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Epidural anesthesia during upper abdominal surgery provides better postoperative analgesia

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Abstract: Since repeated noxious stimuli may sensitize neuropathic pain receptors of the spinal cord, we tested the hypothesis that the appropriate blockade of surgical stimuli with epidural anesthesia during upper abdominal surgery would be beneficial for postoperative analgesia. Thirty-six adult patients undergoing either elective gastrectomy or open cholecystectomy were randomly allocated to receive either inhalational general anesthesia alone (group G) or epidural anesthesia along with light general anesthesia (group E) throughout the surgery. Postoperative pain management consisted of patient-controlled analgesia (PCA) with bupivacaine accompanied by the continuous infusion of buprenorphine. To assess postoperative pain, a visual analogue scale (VAS) was employed at 2, 24, and 48 h postoperatively. While there was no significant difference in the bupivacaine dose, more patients undergoing gastrectomy in group G required supplemental analgesics than those in group E, and the VAS scores in group E demonstrated significantly better postoperative analgesia compared to group G after both types of surgery. Thus, an appropriate epidural blockade during upper abdominal surgery likely provides better postoperative pain relief.

Key words: Epidural anesthesia, Patient-controlled analgesia, Preemptive analgesia, Upper abdominal surgery, Visual analogue scale

Introduction

As a primary obligation of anesthesiologists, pain relief may be the most fundamental and consequential aspect of surgery for patients throughout perioperative periods. Recently, the benefits of regional nerve blockade with local anesthetics during surgery have been intensely appreciated as producing postoperative pain relief [1,2]. Since noxious sensory impulses from injured tissues increase the excitability of the central nervous system, local anesthesia such as infiltration or peripheral nerve blocks prior to surgical incision probably serves to depress the "sensitization" of both central and peripheral nervous systems [1–4]. However, the efficacy of nerve blocks at the level of the spinal cord, i.e., the central nervous system, remains to be determined [5–8]. We designed this study to examine whether spinal cord blockade prior to surgical incision and throughout surgery would demonstrate beneficial consequences on postoperative pain management. More specifically, the aim of the current randomized study was to clarify whether epidural anesthesia during upper abdominal surgery would provide advantageous effects on postoperative pain control and analgesic demands compared to inhalational general anesthesia alone.

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Methods

After obtaining approval from the Institutional Ethics Committee and informed consent from the patients, we studied 36 adult patients undergoing either elective gastrectomy ($n = 18$) or elective open cholecystectomy ($n = 18$). The criteria for exclusion from the study were: ASA physical status rating of III or greater, patients requiring postoperative ventilatory support, or those with neurologic disorders. All patients received 150 mg ranitidine orally at 21:00 the day before surgery, and 50 mg hydroxyzine and 0.5 mg atropine intramuscularly 60 min prior to surgery.

Study protocol

To obviate the confounding factor of surgical variation, the patients undergoing gastrectomy (gastrectomy study) were studied separately from those who under-

went open cholecystectomy (cholecystectomy study). All patients received an epidural catheter (17-gauge, Minikit, Abbott Ireland, Sligo, Ireland) inserted at the T7/8 or T8/9 intercostal level prior to the induction of general anesthesia. The patients were then randomly allocated into two groups: group G (n = 8 in the gastrectomy study and n = 9 in the cholecystectomy study) received inhalational general anesthesia alone, and group E (n = 10 in the gastrectomy study and n = 9 in the cholecystectomy study) received continuous epidural anesthesia with light general anesthesia during surgery.

In group E of both operation studies, 12–15 ml of 1% mepivacaine was epidurally administered prior to the induction of general anesthesia, followed by the continuous infusion of 1% mepivacaine at a rate of 7–10 ml·h^{-1}. The dose of 1% mepivacaine was clinically determined by staff anesthesiologists, mainly based on the patient's condition. All patients then received intravenous administration of thiopental (3–4 mg·kg^{-1}) for induction of general anesthesia, followed by succinylcholine (1 mg·kg^{-1}) to facilitate endotracheal intubation. Anesthesia was maintained with 67% nitrous oxide in oxygen and sevoflurane or enflurane. The end-expiratory concentration of sevoflurane or enflurane was maintained at between 1.5% and 2.5% in group G, and at less than 0.5% in group E throughout surgery, monitored by an anesthesia gas monitor (Capnomac, Datex, Helsinki, Finland). Muscle relaxation was achieved with intermittent injection of vecuronium bromide. For 10 min before and after the surgical incision, systolic blood pressure (SBP) and heart rate (HR) were recorded every minute. These hemodynamic parameters were then monitored every 5 min throughout surgery.

Fifteen to 30 min before completion of the operation, 8–12 ml of 0.25% bupivacaine with buprenorphine (0.1 mg) was epidurally administered to all patients to ascertain the appropriate placement of the epidural catheter. Following emergence from general anesthesia, we assessed the level of sensory analgesia using the pinprick test, and excluded those who could not obtain a blockade higher than the T5 level. Elevation of systolic blood pressure during the operation in group E, defined for each patient using the nomogram on the basis of preoperative blood pressure, was considered to be insufficient epidural blockade [9], and those patients were also excluded from the analysis.

Postoperative pain management and assessment

Postoperatively, the epidural catheter was connected to both a patient-controlled analgesia (PCA) device (Bard, Bard, MA, USA) loaded with 0.25% bupivacaine and a continuous infusion syringe pump (Terfusion, Terumo, Tokyo, Japan) loaded with 0.4 mg of buprenorphine in 48 ml of normal saline. The PCA system allowed a bolus infusion of 3 ml bupivacaine with a lockout time of 30 min, and the infusion pump was set at an infusion rate of 1 ml·h^{-1} (0.008 mg·h^{-1} of buprenorphine) for the next 24 h for the cholecystectomy study and 48 h for the gastrectomy study, respectively. As a supplemental analgesic, pentazocine (15 mg) was given intramuscularly on request by the ward nurses blinded to the study group. To assess the severity of postoperative pain, the patients were asked to rate their wound pain at rest by pointing to the level of pain (by themselves) using a 10-cm visual analogue scale (VAS) graded from 0 cm (no pain) to 10 cm (the most severe pain imaginable) at 2, 24, and 48 h following surgery. The interviewer was unaware of the study design. Adverse effects probably related to anesthesia or postoperative pain management were recorded throughout the study period.

Data analysis

Data are expressed as mean ± SEM unless otherwise specified. The results of VAS were analyzed using analysis of variance (ANOVA) with repeated measurements. When significant differences were found, Bonferroni's corrected paired t-test was employed as post hoc testing. The chi-squared and Mann-Whitney U tests were employed where appropriate. A P value less than 0.05 was considered statistically significant.

Results

Two patients were excluded from group E because the epidural blockade was insufficient during surgery, and two patients (one from each group) were also excluded because of inadequate sensory analgesia obtained after emergence from general anesthesia. All other patients attained an anesthesia level above T5 following emergence.

The demographic data of the patients showed no significant difference between the groups, except for body weight in the gastrectomy study, where body weight in group G was greater compared with group E (Table 1). This significant difference in body weight is due to three patients whose body weights were beyond the range of two standard deviations of all patients. Excluding these three patients, the data showed a nonsignificant body weight difference between the groups and did not change the results of the statistical analyses. Therefore, we believe that the significant differences in the following data are not caused by the body weight difference, and all analyses presented below include the data from those three patients. Total duration of surgery and the

Table 1. Patient characteristics and hemodynamic changes

	Gastrectomy study		Cholecystectomy study	
	Group G ($n = 7$)	Group E ($n = 10$)	Group G ($n = 8$)	Group E ($n = 7$)
Female/male	1/6	5/5	3/5	5/2
Age (years)	59.4 ± 3.1	58.0 ± 3.5	68.1 ± 4.1	53.3 ± 5.8
Weight (kg)	64.8 ± 3.6	52.2 ± 3.0*	56.3 ± 2.5	64.0 ± 4.1
Height (cm)	162 ± 3	156 ± 3	155 ± 3	156 ± 3
Duration of surgery (min)	203 ± 21	212 ± 24	101 ± 16	117 ± 10
Sevoflurane/enflurane (n)	5/2	8/2	6/2	6/1
SBP (mmHg)				
Preincision	116 ± 8	105 ± 5	111 ± 6	110 ± 4
Postincision	140 ± 8**	105 ± 6	136 ± 8**	111 ± 7
HR (beats/min)				
Preincision	76 ± 3	81 ± 5	72 ± 3	82 ± 5
Postincision	81 ± 4	84 ± 6	78 ± 2	81 ± 5

SBP, systolic blood pressure; HR, heart rate.
Values are mean ± SEM. Group G, general anesthesia group; group E, epidural anesthesia group.
* $P < 0.05$ versus group G in the same operation study. ** $P < 0.05$ versus preincision in the same subgroup.

Table 2. Analgesics required during postoperative periods

	Gastrectomy study		Cholecystectomy study	
	Group G ($n = 7$)	Group E ($n = 10$)	Group G ($n = 8$)	Group E ($n = 7$)
Total bupivacaine dose by PCA (ml)	54.6 ± 9.7	57.6 ± 11.0	31.8 ± 4.1	29.7 ± 8.2
Pentazocine (mg)	35.0 ± 15.3	5.6 ± 3.9*	11.3 ± 7.9	0

Group G, general anesthesia group; group E, epidural anesthesia group; PCA, patient-controlled analgesia.
Values are mean ± SEM.
* $P < 0.05$ versus group G in the same operation study.

choice of sevoflurane or enflurane did not differ between the groups in each operation (Table 1).

While the systolic blood pressure (SBP) in group E did not change after skin incision (Δ percent change: −4% in the gastrectomy study and ±0% in the cholecystectomy study), the patients in group G showed a significant increase in SBP immediately following the skin incision (Δ: +21% in the gastrectomy study and +24% in the cholecystectomy study) (Table 1). The heart rate after skin incision did not change between the groups in each operation study (Table 1).

Table 2 shows the total doses of the analgesics required during the postoperative period. There was no significant difference in bupivacaine dose for PCA between the groups in both operation studies. However, more intramuscular pentazocine was given in group G versus group E in the gastrectomy study. The percentage of patients requiring pentazocine was significantly greater in group G versus group E in the gastrectomy study (83.3% *vs* 11.1%; $P < 0.01$). On the other hand, there was no significant difference in either bupivacaine dosage during the PCA period, total dose of pentazocine, or the number of patients who required an additional analgesic between groups G and E in the cholecystectomy study.

The VAS scores across the evaluation periods are depicted Figs. 1 and 2. In the gastrectomy study, significantly greater analgesia was observed in group E throughout the postoperative period versus group G, while the scores in both groups were significantly lower (i.e., better) from 2h to 24 and 48h following surgery (Fig. 1). In the cholecystectomy study, the VAS scores in group E were significantly better throughout the study period compared to group G, and furthermore those at the 48-h period demonstrated significantly lower (= better) scores versus both 2- and 24-h periods (Fig. 2). The VAS scores of group E in the cholecystectomy study were lower (= better) than those of the same anesthesia group in the gastrectomy study. Between the two operations in group G, however, no significant differences were found.

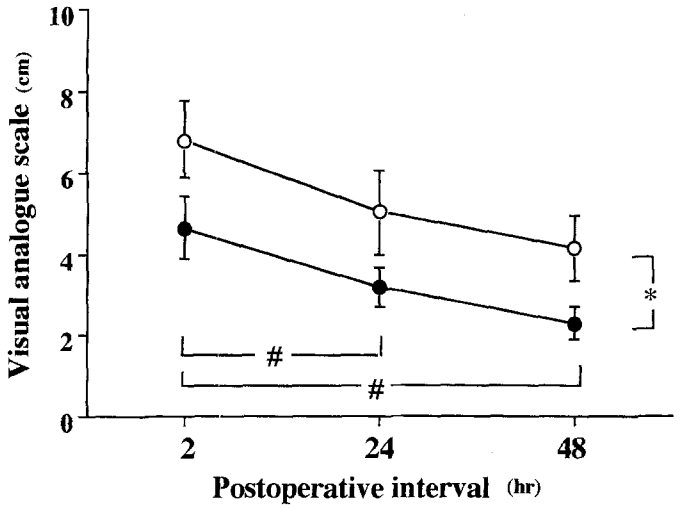

Fig. 1. Evaluation of postoperative analgesia by visual analogue scale (*VAS*) at rest in the gastrectomy study. Values are mean ± SEM. Group G (*open circles*), general anesthesia group; group E (*solid circles*), epidural anesthesia group. Significance of data: $^{*}P < 0.05$ between the two groups throughout the study period. $^{\#}P < 0.05$ between the different evaluation periods. No significant interaction [group × time] was found by multiple analysis of variance with repeated measures

Discussion

Since potent nociceptive signals are generated not only by the surgical procedure but also by the action of inflammatory mediators released into the wound tissues [3,8], local infiltration of long-lasting anesthetics may be able to offer better protection to the central nervous system from noxious stimuli than a nerve blockade at the level of the spinal cord. Indeed, Tverskoy and co-workers [1] showed that the infiltration of local anesthetics with general anesthesia during inguinal herniorrhaphy resulted in further suppression of postoperative pain compared to spinal anesthesia. Several previous studies demonstrated the beneficial outcome of epidural analgesia with or without opioids, steroids, or other analgesics given to attenuate postoperative pain [10–12]. However, few studies have explicitly examined the validity of sufficient epidural anesthesia employed prior to surgical incision and throughout major abdominal surgery [4,6,12–14]. Although the cumulative dose of bupivacaine with the PCA system was not significantly different between the groups, the VAS scores and the supplemental analgesic demands showed an obviously more effective postoperative analgesia in group E versus group G, with the exception of supplemental analgesic requirements in the cholecystectomy study. Thus, this study indicates that the appropriate use of epidural blockade throughout upper abdominal surgery provides greater postoperative analgesia than inhalational general anesthesia alone.

Compared with previous studies, our study design is characterized by the following features. First, single or intermittent blockade may not be sufficient to prevent noxious stimuli from entering the spinal cord during surgery. Woolf [8] suggested that intraoperative epidural local anesthetic treatment in previous studies was not adequate to block afferent impulses to prevent central sensitization. Thus, a longer-term, satisfactory dose of local anesthetics such as that administered in this study is probably associated with more distinct beneficial effects of the epidural blockade on postoperative pain relief. Second, we performed more stressful surgery while previous studies have focused on relatively minor surgery [1,2,5,15,16]. Postoperative pain management is usually the most difficult in patients after major abdominal surgery, especially upper abdominal surgery, compared with lower abdominal surgery or surgery of the extremities. Furthermore, even among upper abdominal surgery patients, cholecystectomy produced less postoperative pain stress than gastrectomy, as verified by the higher VAS scores of group E in the gastrectomy compared to the cholecystectomy study. Thus, the significant difference in VAS scores could be more apparent during movement compared with at rest. Third, the quality of premedication should also be considered when planning a study protocol. Morphine 10 mg given as premedication has been reported to depress postoperative pain and analgesic requirements [16]. Since a combination of hydroxyzine with atropine alone was given as premedication, we assume that the

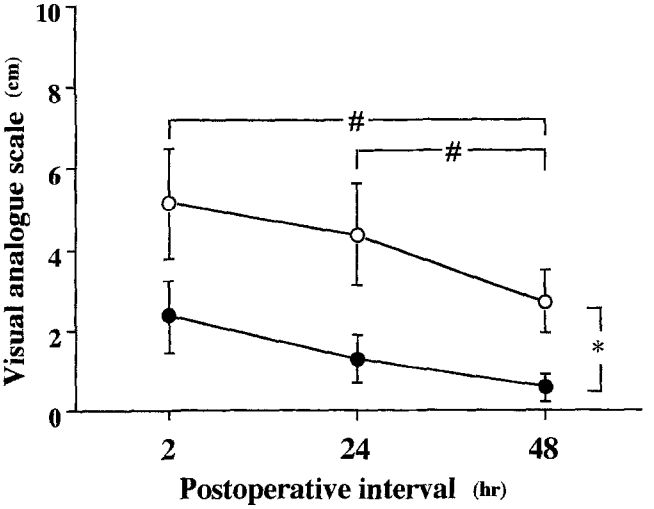

Fig. 2. Evaluation of postoperative analgesia by visual analogue scale (*VAS*) at rest in the cholecystectomy study. Values are mean ± SEM. Group G (*open circles*), general anesthesia group; group E (*solid circles*), epidural anesthesia group. Significance of data: $^{*}P < 0.05$ between the two groups throughout the study period. $^{\#}P < 0.05$ between different evaluation periods. No significant interaction [group × time] was found by multiple analysis of variance with repeated measures

premedication in this study had minimal effects on postoperative pain. Finally, we believe that the timing of epidural blockade was of great consequence. In the current study, we employed epidural anesthesia prior to surgical incision and then continuously administered a local anesthetic to prevent noxious stimuli throughout surgery. In previous studies, where no benefits of epidural anesthesia were suggested in terms of postoperative pain relief, sufficient epidural blockade may not have been achieved throughout surgery [6,7]. As to the apparent advantage of infiltrated local anesthetics previously reported [1,2], it may be of importance to achieve complete nerve blockade prior to any surgical stimuli so as to obtain preemptive analgesia. Recently, Shir and co-workers [17] reported that epidural anesthesia during radical prostatectomy produced less postoperative pain and lower analgesic requirements compared with either general anesthesia alone or combined epidural and general anesthesia. Our study further indicates that an appropriate blockade of noxious stimuli may be able to ensure less postoperative pain even in patients undergoing major abdominal surgery.

It could be argued that epidural anesthesia during surgery was indeed sufficient to protect the spinal cord from repeated noxious stimuli. Since we employed general anesthesia for reasons of clinical safety, it was not possible to monitor the level of epidural blockade area during surgery. In order to verify that sufficient epidural blockade was obtained during the operation, the concentration of inhalational analgesics was limited to a minimum, so that the airway irritability caused by placement of the endotracheal tube was suppressed. We then administered more mepivacaine than clinically considered adequate by staff anesthesiologists prior to the surgical incision, followed by continuous infusion to avoid reduction of the blockade area. Furthermore, we excluded three patients in group E from this study owing either to their unstable hemodynamic changes during surgery or to insufficient sensory analgesia obtained after emergence from general anesthesia. Given these rationale, we believe that epidural anesthesia in the current study was able to obtain fairly close to complete suppression of noxious stimuli at the spinal cord level.

Another controversial issue in this type of study is how postoperative pain should be assessed properly. Among several methods previously reported, the visual analogue scale (VAS) is considered to be the most reliable in reflecting the pain condition [8,18]. Although there is no doubt that this test is not objective in evaluating the patients' pain, we believe that the most uncomfortable sensory signals should be assessed not by the observer's impression but primarily by the patients' subjective feeling. Furthermore, since not all patients are ready to be interviewed for the VAS score sheet shortly after the operation, we considered it more practical to assess the pain state 2h following the operation, by which time bupivacaine administered epidurally prior to the completion of surgery would no longer be effective.

For postoperative pain management, we used a PCA device which has recently come into widespread use [18,19]. Since the application of PCA allows the patient himself/herself to titrate analgesics to his/her own demand, its setting may be more objective as an estimate of the patients' pain state than other analgesic methods [8,20]. Shir's study [17] suggested that PCA demand could be taken as evidence of postoperative analgesic requirements. In contrast to the previous study and the VAS scores in the current study, however, the total requirements of bupivacaine as shown by the PCA system were not different between the groups. The reason for this finding might be that, to be clinically secure, we set a limit to the injection dose of bupivacaine with a lockout time in the PCA device. Although we did not record how many times the patients actually pushed the button of the PCA device, the higher demand for supplemental pentazocine injection in group G suggests that the true requirement for PCA could have been greater in group G compared to group E.

In conclusion, the use of appropriate epidural blockade prior to surgical stimuli and throughout surgery reduces wound pain and supplemental analgesic requirements during the first 48h following upper abdominal surgery.

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