

# Quality of Postoperative Pain Using an Intraoperatively Placed Epidural Catheter after Major Lumbar Spinal Surgery

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**Background:** Major spinal surgery is associated with high postoperative pain scores and opioid requirement. The aim of the current prospective, randomized, placebo-controlled, double-blind study was to assess the reduction of opioid requirement and pain scores using an intraoperatively placed epidural catheter with infusion of 0.1% ropivacaine during the postoperative period.

**Methods:** Thirty patients undergoing major lumbar spinal surgery from a dorsal approach were included in this study. Before wound closure, the orthopedic surgeon inserted an epidural catheter. Postoperatively, patients were randomly assigned to receive an infusion of 12 ml/h ropivacaine, 0.1% (group R), or 12 ml/h saline (group N) after an initial bolus of 10 ml of the respective study solution. Additional pain relief was provided using an intravenous patient-controlled analgesia pump with the opioid piritramide. Patients were assessed with respect to pain scores (visual analog scale of 0–100), cumulative opioid requirement, side effects, and satisfaction with pain management.

**Results:** Demographic data, duration of surgery, and type of surgery were comparable between groups. Pain scores were assessed as follows (group R vs. group N: 6 h:  $24 \pm 20$  vs.  $51 \pm 20$ ,  $P = 0.002$ ; 24 h:  $33 \pm 19$  vs.  $53 \pm 27$ ,  $P = 0.04$ ; 48 h:  $21 \pm 17$  vs.  $40 \pm 26$ ,  $P = 0.04$ ; 72 h:  $14 \pm 13$  vs.  $38 \pm 25$ ,  $P = 0.02$ ). The cumulative piritramide requirement after 72 h was  $97 \pm 23$  mg in group R and  $157 \pm 72$  mg in group N ( $P = 0.03$ ). The incidence of side effects was comparable between groups, and patient satisfaction was always higher in group R ( $P < 0.05$ ).

**Conclusion:** Continuous epidural infusion of 0.1% ropivacaine results in lower pain scores and opioid consumption and higher patient satisfaction when compared with placebo. Application of ropivacaine using an epidural catheter seems to be a highly effective treatment for postoperative pain after major lumbar spinal surgery.

PATIENTS undergoing spinal surgery experience severe pain in the postoperative period, which may increase morbidity and incidence of complications and prolong postoperative rehabilitation. In addition, postoperative pain itself is a risk factor for development of chronic

pain syndromes.<sup>1,2</sup> Postoperative pain therapy mainly exists in application of oral or intravenous opioids in combination with nonsteroidal antiinflammatory drugs, but it often results in insufficient pain control and side effects such as respiratory depression, nausea, and vomiting.

Epidural anesthesia and analgesia have been shown to be superior to intravenous analgesia with respect to pain quality, incidence of side effects, and pulmonary, cardiac, and gastrointestinal dysfunction.<sup>3,4</sup> Turner *et al.*<sup>5</sup> showed in an observational study that epidural catheters placed intraoperatively by the surgeon followed by infusion of local anesthetics with or without opioids were capable of providing good analgesia after posterior spinal fusion. Apart from dislocation, the placement of an epidural catheter into a recently operated area in the vertebral column with epidural application of local anesthetics may include the problem of unpredictable absorption of the drug and motor blockade.

Therefore, we designed this prospective, randomized, double-blind, placebo-controlled study to evaluate the analgetic effect and side effects of postoperative continuous epidural infusion of 0.1% ropivacaine using an epidural catheter placed intraoperatively by the surgeon in patients undergoing major lumbar spinal surgery. Plasma concentrations of unbound ropivacaine were measured to control systemic absorption of the local anesthetic.

## Materials and Methods

After approval of the local ethics committee (Hamburg, Germany) and written informed consent were obtained, 30 adult patients undergoing major lumbar spinal surgery from a dorsal approach were included in the study within a period of 8 months. The surgical procedure consisted of dorsal or dorsoventral fusion of the lumbar vertebral column. Exclusion criteria consisted of allergy against local anesthetics, American Society of Anesthesiologists physical status class greater than III, infection in the area of the operation, postoperatively need for artificial ventilation for more than 2 h, operation of the cervical or thoracic spine, neurologic deficits, spinal metastasis, and preexisting pain symptoms apart from back pain associated with the planned operation.

On the day before surgery, patients were examined with respect to preoperative pain scores and hemody-

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dynamic variables. In addition, patients were introduced to the use of an intravenous patient-controlled analgesia (PCA) pump. On the day of surgery, patients were premedicated with 0.1 mg/kg midazolam (Hoffmann La-Roche, Grenzach-Wyhlen, Germany). A venous line was inserted in the right or left forearm, and infusion of 500 ml Ringer's solution (lactated) was started. Anesthesia was induced with 0.5  $\mu$ g/kg sufentanil (Janssen-Cilag, Neuss, Germany) and 2 mg/kg propofol (AstraZeneca, Wedel, Germany). Tracheal intubation was facilitated with 0.5 mg/kg rocuronium bromide (Organon, Oberschleißheim, Germany). Maintenance of anesthesia was performed with additional application of 0.1  $\mu$ g/kg sufentanil and 4–5 vol% desflurane with a fraction of inspired oxygen ( $F_{IO_2}$ ) of 0.3 in air. Normothermia was maintained with forced air. In addition, a central venous line was inserted into the external or internal jugular vein for central venous blood gas measurement. An arterial line was introduced in the left or right radial artery for assessment of arterial blood pressure, and a urinary catheter was placed for control of diuresis. Operation was performed in the prone position. If additional ventral fusion was necessary, the patient was turned in the supine or lateral position.

At the end of the posterior surgical procedure, a multihole epidural catheter (B. Braun, Melsungen, Germany) was placed by the orthopedic surgeon either under direct vision when epidural space was opened during surgery or with the loss-of-resistance technique using an 18-gauge Tuohy needle. The catheter then was tunneled through the subcutaneous tissue, and the intact skin and was secured with a single surgical knot. Catheters were always placed in the middle of the operation field and introduced 3 cm into the epidural space. After closure of the subcutaneous tissue, a mechanical pump (Pegasus GmbH, Kiel, Germany) was connected to the epidural catheter, and a 10-ml bolus of the respective study solution was infused through the epidural catheter. The study medication was delivered by the hospital's pharmacy department in bags containing 300 ml of the respective study solution. According to the computerized randomization list, the pharmacist filled the bags with 300 ml ropivacaine, 0.1% (AstraZeneca), in group R or saline in group N under sterile conditions. A sticker on the bag contained the following information: patient initials, patient number in the study (number 1–30), and the information that the bag contained study solution. Bags of both study groups appeared identical. A closed envelope with information about the patient's study medication (0.1% ropivacaine or saline) was added in the patient's record for emergency cases. All persons involved in the study were blinded to the study medication, except the pharmacist filling the bag with the study solution.

After application of the initial bolus, a continuous infusion of 12 ml/h ropivacaine, 0.1%, in group R or

12 ml/h NaCl, 0.9%, in group N was started to provide sufficient perfusion of the epidural space. Infusion was continued until 72 h postoperatively. After the end of the operation, patients were extubated and transferred to the postanesthesia care unit. The intravenous PCA pump was connected to the central venous line, and the patient was asked to use the pump whenever pain was experienced. The PCA medication consisted of a bolus of 1.5 mg of the  $\mu$ -receptor agonist piritramide (15 mg piritramide is equivalent to 10 mg morphine).<sup>6</sup> The lock-out time of the PCA pump was 5 min, and the 4-h maximum was 22.5 mg piritramide for safety reasons. Patient-controlled epidural analgesia was avoided because the use of two hand-operated devices (patient-controlled epidural analgesia and intravenous PCA) could confuse the patients.

One, 2, 4, 6, 24, 36, 48, 60, and 72 h after surgery, patients were examined with respect to visual analog scale (VAS) values on a scale from 0 and 100, cumulative piritramide requirements, and hemodynamic parameters such as heart rate, blood pressure, and oxygen saturation (pulse oximetry). Body core temperature was measured in the auditory canal with a tympanic probe. Side effects included nausea and vomiting, shivering (only until 24 h after surgery), and assessment of a sedation score (1 = patient awake, 2 = patient easy to awake, 3 = patient difficult to awake, 4 = patient impossible to awake). Intensity of motor blockade was assessed using the Bromage scale (0–3). In addition, patients were asked about any kind of paresthesia. Patient satisfaction with the pain management was assessed using a six-point scale (1 = very good, 2 = good, 3 = satisfactory, 4 = sufficient, 5 = unsatisfied, 6 = very unsatisfied). This instrument has not been validated before. The anesthesiologist performing these postoperative examinations was blinded to the study medication, too.

Venous blood was sampled for measurement of total and unbound ropivacaine plasma concentrations before induction of anesthesia and 6, 24, 48, and 72 h after surgery. Blood was immediately centrifuged for 10 min at 3,000 rotations/min. The resulting plasma samples were frozen at  $-20^{\circ}\text{C}$ . Ropivacaine plasma concentrations were evaluated by high-pressure liquid chromatography with ultraviolet detection as described previously.<sup>7</sup> The accuracy of the assay is nearly 95%, and the confidence interval is  $\pm 1.25\%$ .

After the study period of 72 h, epidural catheters were removed, and analgesia was continued with PCA if necessary.

#### Statistical Analysis

For sample size calculation, the mean VAS value 6 h after surgery was expected to be around 55 mm based on evaluation of patients before start of the study. Using 0.1% ropivacaine for epidural application, we expected to achieve a mean VAS value of 30 mm. The anticipated

**Table 1. Demographic and Perioperative Data**

	Group N (n = 13)	Group R (n = 13)	P Value
Age, yr	54.8 ± 17	58.1 ± 16	0.61
Height, cm	167 ± 10	173 ± 15	0.23
Weight, kg	76.3 ± 19	77.7 ± 19	0.85
Sex, M/F	7/6	8/5	0.69
ASA physical status, I/II/III	2/7/4	2/8/3	0.9
Duration of anesthesia, min	406 ± 82	396 ± 138	0.79
Duration of surgery, min	322 ± 75	308 ± 137	0.75

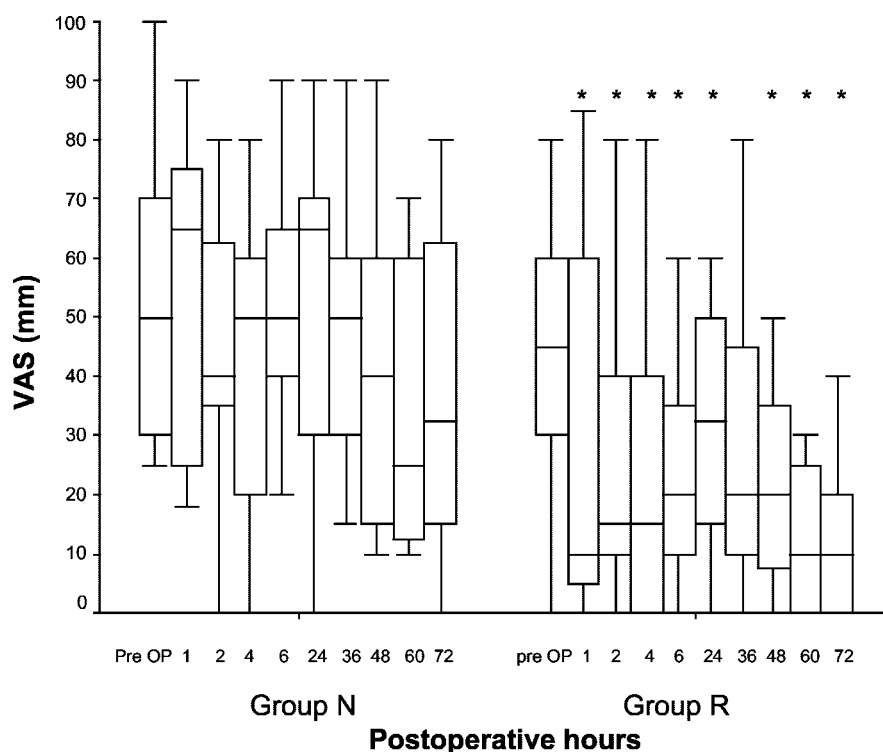
ASA = American Society of Anesthesiologists.

pooled SD was set at 20 mm of the VAS values. We would permit a type I error of  $\alpha = 0.05$ , and with the alternate hypothesis, the null hypothesis would be retained with a type II error of  $\beta = 0.2$ . This reaches a power of 0.8 and indicated that a sample size of at least 12 patients/group was necessary (Instat; Graphpad, San Diego, CA). On the background of possible dropouts from statistical analysis, a sample size of 15 patients/group was chosen.

Computerized statistical analysis was performed using the program SPSS 9.0 (SPSS Inc., Chicago, IL). Differences between groups were compared using the unpaired Student *t* test (cumulative piritramide requirement, patient satisfaction). VAS values were tested using the Mann-Whitney U test. Incidences of side effects were compared using the chi-square test. Data are expressed as mean ± SD or incidences if not otherwise declared.  $P < 0.05$  was considered to be statistically significant.

## Results

Four of the 30 patients included in the study dropped out from the statistical analysis. In group R, 1 patient was excluded because of accidental perforation of the dura during surgery, and 1 patient of each group was excluded because of impossibility to introduce the epidural catheter due to extensive epidural fibrosis after previous spinal surgery. Patients with preceding spinal surgery were then excluded from further study. The other patient in group N was excluded because of catheter dislocation in the postanesthesia care unit. One patient in each group used opioids preoperatively; application was stopped on the evening before surgery. In group N, 9 patients underwent surgery with use of a combined dorsoventral approach, and 4 had a single dorsal approach, whereas 7 patients in group R needed a dorsoventral approach, and only 6 patients had the dorsal approach ( $P = 0.27$ ). In 12 patients (6 in each group), the epidural space was not opened during surgery, and



**Fig. 1.** Visual analog scale (VAS) values. Data are presented as median, interquartile range, and range (\*  $P < 0.05$  vs. group N).

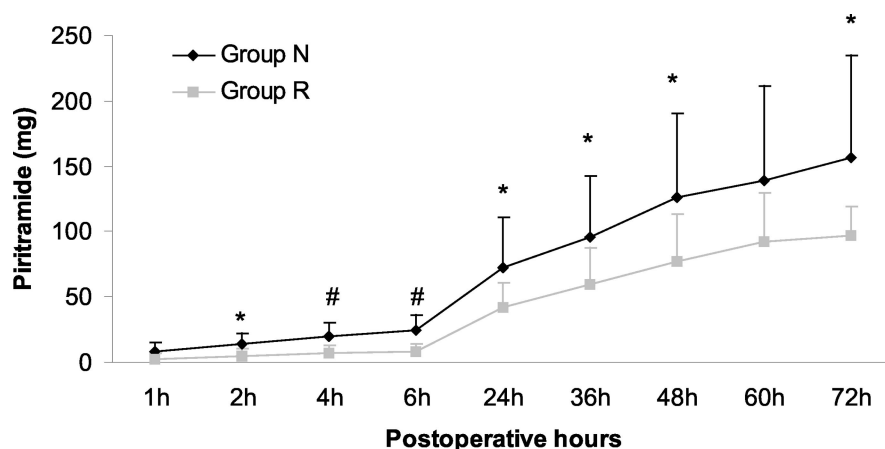


Fig. 2. Cumulative piritramide requirement (\* $P < 0.05$ , # $P < 0.005$  vs. group R).

the epidural catheter had to be placed using the loss-of-resistance technique. Postoperatively, 1 patient in each group was transferred to the intensive care unit because of preexisting cardiovascular disease.

As shown in table 1 demographic data were comparable with respect to age, sex, body weight and height, American Society of Anesthesiologists physical status, and duration of surgery and anesthesia. The preoperative VAS values were high but comparable between the study groups (fig. 1). Continuous epidural infusion with 0.1% ropivacaine resulted in significant reduction in VAS values during the whole study period. Only 36 h after surgery were differences not significant. Cumulative piritramide requirement is shown in figure 2. Patient satisfaction was higher during the whole study period in

patients receiving epidural ropivacaine (fig. 3). Hemodynamic parameters such as heart rate and blood pressure were comparable between groups during the whole study period. Body temperature and oxygen saturation showed no differences between groups, either. The incidence of side effects is shown in table 2. In addition, sedation score was not different between groups. The following results show sedation scores 3 and 4, which are clinically relevant (sedation score 3/4 [number], group N vs. group R): 6 h: 3/0 versus 1/0; 24 h: 1/0 versus 0/0; 36 h: 1/1 versus 0/0; 48 h: 1/0 versus 0/0; 60 h: 1/0 versus 0/0; 72 h: 0/0 versus 0/0.

No clinical symptoms of local anesthetic intoxication were detected until the end of the study period. The plasma concentrations of unbound ropivacaine in group

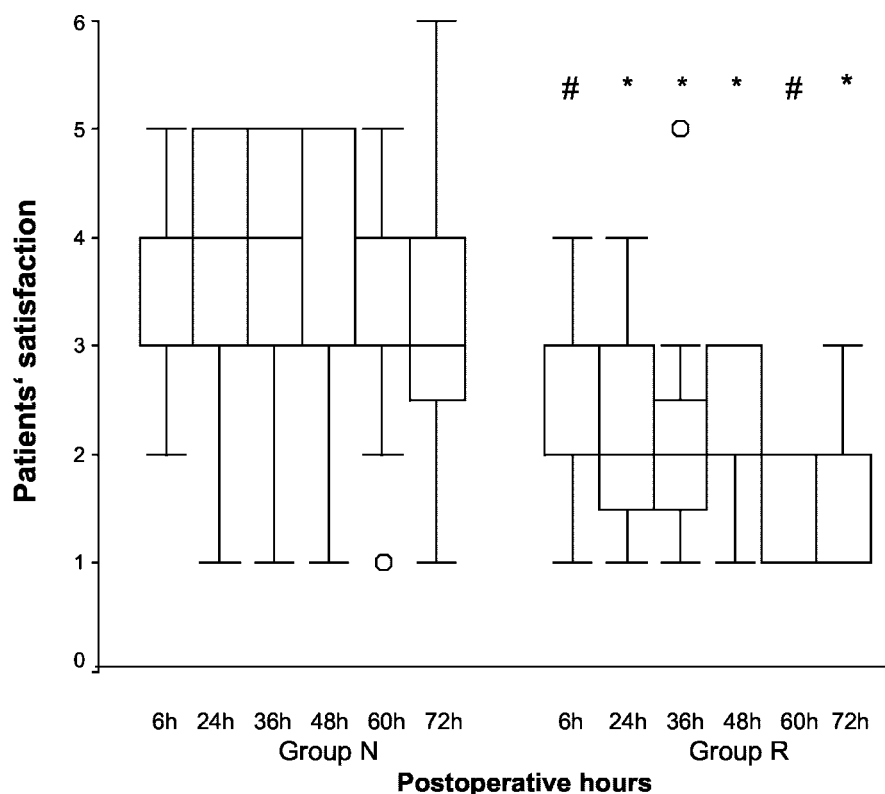


Fig. 3. Patients' satisfaction (1 = very good, 6 = very unsatisfied; \* $P < 0.05$ , # $P < 0.005$  vs. group N). Data are presented as median, interquartile range, range, and outliers (o).



Table 2. Incidence of Side Effects

	Group N vs. Group R					
	6 h	24 h	36 h	48 h	60 h	72 h
Bromage > 1, n	0 vs. 0	0 vs. 0	0 vs. 0	0 vs. 0	0 vs. 0	0 vs. 0
Nausea, n	3 vs. 5	4 vs. 3	3 vs. 5	2 vs. 3	4 vs. 3	1 vs. 4
Vomiting, n	2 vs. 3	3 vs. 3	2 vs. 4	0 vs. 1	3 vs. 1	1 vs. 2
Shivering, n	2 vs. 1	1 vs. 0				
Paresthesia, n	1 vs. 7*	2 vs. 7*	0 vs. 5*	0 vs. 5*	0 vs. 5*	0 vs. 3*

\*  $P < 0.05$ .

n = number of patients.

R always remained below the toxic threshold of  $0.6 \mu\text{g/ml}$  (values are given as median and minimum-maximum values): preoperative: 0.0, 0.0–0.0  $\mu\text{g/ml}$ ; 6 h: 0.017, 0.0–0.14  $\mu\text{g/ml}$ ; 24 h: 0.014, 0.0–0.03  $\mu\text{g/ml}$ ; 48 h: 0.01, 0.0–0.03  $\mu\text{g/ml}$ ; 72 h: 0.004, 0.0–0.05  $\mu\text{g/ml}$ ). As expected, in group N, no ropivacaine plasma concentrations could be measured. No patient showed any sign of local infection at the catheter site or wound healing problems.

## Discussion

Continuous postoperative infusion of 0.1% ropivacaine using an epidural catheter placed intraoperatively by the orthopedic surgeon resulted in significant reduction of pain scores, reduced requirement of additional opioids, and a higher patient satisfaction after major lumbar spinal surgery. To our knowledge, this is the first prospective, randomized, double-blind study using an intraoperatively placed epidural catheter with continuous postoperative infusion of a local anesthetic that is placebo controlled. In addition, analgetic effects were assessed not only by using the VAS values, but also by providing a patient-controlled intravenous pump for additional pain relief and objective evaluation of opioid requirement.

The only comparable study was performed by Cohen *et al.*<sup>8</sup> with two groups of adult patients who all received an epidural catheter and a patient-controlled intravenous analgesia delivery system. Patient-controlled intravenous (morphine) or epidural analgesia (0.0625% bupivacaine–0.004% morphine) was performed in a double-blind manner. In contrast to our study, there were no significant differences between the epidural and intravenous PCA groups at any time after surgery. One possible reason for the lack of effect may be that epidural catheters were placed two to three levels cephalad to the operative level. As already mentioned by Brennan,<sup>9</sup> it is essential, when local anesthetics are used, that the medication is delivered to the spinal nerve roots innervating the tissue injured by surgery. Therefore, we placed our catheter in the middle of the operation field and introduced it 3 cm in cranial direction. In addition, we used a high infusion

rate of 12 ml/h, which should provide sufficient local anesthetic distribution.

In 10 patients undergoing anterior spinal fusion for adolescent scoliosis, Lowry *et al.*<sup>10</sup> performed a prospective review of the effects of an epidural catheter with postoperative infusion of 0.1% ropivacaine in combination with hydromorphone (10  $\mu\text{g/ml}$ ) at an infusion rate of  $0.2 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ . Persistent pain was treated with a bolus and a 20% increase of the epidural medication (severe pain), ketorolac or diazepam (mild to moderate pain). Pain values in this study were slightly lower than the pain scores we achieved in our study, but because a control group was not included, the effects of the performed therapy are difficult to estimate. Compared with the study of Lowry *et al.*, patients in our group did not have to wait for any personal for application of additional analgetics or application of an epidural bolus but were able to use the intravenous PCA device whenever necessary.

Different studies have been performed with the epidural application of opioids. Joshi *et al.*<sup>11</sup> compared two groups of patients: The epidural group received continuous fentanyl infusion (2  $\mu\text{g/ml}$ ; 4–10 ml/h), whereas the intravenous PCA group received morphine. The study resulted in superior pain relief in patients receiving epidural fentanyl. Preemptive epidural morphine was found to be superior in comparison to postoperatively administered epidural morphine in patients undergoing lumbar laminectomy.<sup>12</sup>

Since safety of epidural analgesia has been shown in children, several studies have been performed demonstrating good analgetic effects of epidural analgesia after spine surgery.<sup>13,14</sup> In contrast, Cassady *et al.*<sup>15</sup> were not able to show an effect in terms of pain reduction of 0.125% epidural bupivacaine in combination with 0.0025 mg/ml fentanyl compared with intravenous PCA with morphine. Unfortunately, the study was not performed in a double-blind manner.

In our study, we only used the local anesthetic ropivacaine, 0.1%, for epidural analgesia. This low concentration of ropivacaine was chosen to avoid any kind of motor blockade in the lower extremities. After spinal surgery, any motor blockade due to epidural analgesia should be strictly avoided because postoperative hema-

toma with the development of paralysis due to compression of the spinal cord or cauda equina may not be detected. Even with this very low concentration of ropivacaine, nearly 50% of our patients showed paresthesia in the lower extremities. To provide sufficient distribution in the epidural space, an infusion rate of 12 ml/h was chosen. The high infusion rate is probably the main reason we were able to show this analgetic effect after vertebral surgery. Even when the epidural space was disrupted during surgery, local anesthetic that leaks out from epidural space acts somehow like wound infiltration. Wound infiltration after spine surgery has been shown to be effective, as well.<sup>16</sup>

An indispensable condition for clinical settings where epidural catheters are placed directly into the surgical field is good cooperation and communication with the respective surgeons. It is easy to understand that surgeons are afraid of development of any kind of infection of the wound or the epidural space, especially after spine surgery, because even small hematomas are an excellent medium for bacteria. At first glance, a catheter directly placed in this area does not gain acceptance in the eyes of the surgeons, irrespective of the applied medication.

One problem in providing epidural pain management after spinal surgery is probably, as we were able to see, previous spinal operations with epidural fibrosis leading to the impossibility of introducing the epidural catheter. However, this is only a problem for patients who require the loss-of-resistance technique. When the epidural space has to be opened during the surgical decompression procedure, the catheter placement is not a problem, but epidural spread of the respective medication may be unpredictable. In one patient, the dura was accidentally injured during surgical decompression. We avoided placing an epidural catheter in this patient because we could not rule out that the infused local anesthetic may cause complete spinal anesthesia.

In conclusion, our prospective, randomized, double-blind, placebo-controlled study demonstrated significant pain relief and lower opioid requirement during a postoperative time of 72 h after lumbar spinal surgery when compared with intravenous PCA. Side effects were low, the plasma concentrations of unbound ropivacaine remained under the toxic threshold, and patient satisfac-

tion was significantly higher than in the control group. Further studies should examine whether the addition of opioids such as sufentanil or a low-dose *N*-methyl-D-aspartate-receptor antagonist such as *S*(+)-ketamine to the local anesthetic can further improve the achieved pain relief and inhibit the development of chronic pain syndromes.<sup>1,2</sup>

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