Epidural Anesthesia and Analgesia in Liver Resection

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Continuous epidural anesthesia and analgesia has become an accepted technique used in liver resections (1). Liver surgery, however, may cause postoperative coagulation disturbances, even in patients with normal preoperative coagulation function undergoing uncomplicated hepatectomy (2,3), raising concerns about the safety of this technique. Vandermeulen et al. (4) reported that both catheter removal (the physical process) and the patient's coagulation status at the time of removal are critical factors in the development of spinal hematoma. The extent of liver resection may affect the magnitude and duration of postoperative coagulation disturbances (2), and therefore the proper timing of epidural catheter removal. In this study, the safety of epidural catheters in patients undergoing hepatic resections was examined. In addition, the coagulation profile was prospectively compared in patients undergoing minor or major liver resection under combined general-epidural anesthesia.

Materials and Methods

After IRB approval and informed consent, we prospectively studied consecutive patients undergoing hepatic resection, who had no preexisting coagulopathies, and did not require a perioperative transfusion of blood or blood products. All operations were performed by the same two surgeons under standardized general and epidural anesthesia. Epidural catheters were placed at T9-12 interspaces before anesthesia, and a test dose of lidocaine was injected. General anesthesia was induced with fentanyl, thiopental, and vecuronium, and after tracheal intubation, maintained with isoflurane in a 50% oxygen-nitrous oxide balance. A bolus of 10–12 mL of lidocaine 2% with 2 μg/kg fentanyl was administered epidurally. Additional epidural fentanyl and IV muscle relaxant were administered as appropriate. No further local anesthetic drug was given during the intraoperative period. Epidural analgesia (continuous epidural infusion of 16 mg of methadone and 45 mg of bupivacaine [0.5%] over 24 h)] was continued in all patients postoperatively. Epidural catheters were removed when patients had normal coagulation profiles, and platelets $>50 \times 10^3/mm^3$. Patients were classified according to the extent of resected liver: minor resections ($n = 71$) included uni- and bisegmentectomies and nonanatomical resections; major resections ($n = 65$) included all resections that involved 3 or more segments. The weights of the resected specimen were 231 ± 176 and 894 ± 365 g, in the minor and major resections, respectively. Data collected prospectively included age, sex, operation performed, length of operation, volume of intraoperative blood loss, and day of epidural catheter removal. All patients were observed daily for signs of spinal cord compromise. Blood tests, including complete blood count, prothrombin time (PT), activated partial thromboplastin time, and fibrinogen, were determined preoperatively, immediately on admission to the recovery room, daily until the third postoperative day (POD), and every other day until discharge. Measurements of fractionated D-dimer were performed when fibrinogen level was <200 mg/dL.

Differences between the two groups were compared by using the Student's *t*-test. Data within each group were analyzed by using analysis of variance for repeated measurements. When appropriate, *post hoc* analyses were performed with the Newman-Keuls test. The correlation between coagulation and platelet variables and the extent of resected specimen was studied by using Spearman's rank test. Analysis was performed by using Statistical Analysis System software (version 6.12; SAS Institute, Cary, NC). A $P < 0.05$ was considered to represent statistical significance. Results were expressed as the mean ± SD.

Results

One hundred thirty-six consecutive patients, undergoing elective hepatic resection for primary ($n = 13$), metastatic ($n = 99$), or benign tumors ($n = 24$) were studied. There were 59 men and 77 women in the study with a mean age of 61 ± 13 yr (range, 24–81 yr).

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Difficulty (multiple attempts) in needle/catheter placement was present in 6 patients (4%). In 7 patients (5%), blood was noted during needle or catheter placement. The presence of blood during needle or catheter placement did not postpone surgery. Operating time was 152 ± 31 and 297 ± 57 min, and estimated intraoperative blood loss averaged 445 ± 276 and 885 ± 432 mL in the Minor and Major Resection groups, respectively. There were no significant differences between the two groups in preoperative blood tests. In both groups, the PT (expressed in percent) decreased significantly immediately after the operation and reached a nadir on POD 1 (Fig. 1). The changes in PT remained significant until PODs 1 and 5 in the Minor and Major Resection groups, respectively. In the postanesthesia care unit and on PODs 1, 2, and 3, abnormal PT values were found in 68%, 72%, 50%, and 33% of the patients in the Major Resection group, respectively. The corresponding numbers for the Minor Resection group were 28%, 39%, 16%, and 6%, respectively. In addition, by POD 5, PT was <60% in 1 patient (1.4%) in the Minor Resection group compared with 8 patients (12%) in the Major Resection group ($P < 0.05$). A significant decrease in platelet count was observed in the Major Resection group only (Fig. 2). It reached a nadir on POD 3 ($176 \pm 75 \times 10^3/mm^3$) and returned to preoperative value by Day 5. Also in this group, the minimal platelet count was $<100 \times 10^3/mm^3$ in 3 patients (5%) on POD 3 and in 1 patient (1%) on POD 5. None of the patients had a platelet count $<50 \times 10^3/mm^3$. A significant inverse correlation was found between PT, or platelet count, and the weight of liver tissue removed ($r_s = -0.68$ and -0.60, respectively). Partial thromboplastin time and serum fibrinogen levels did not change significantly in the postoperative period. The fibrinogen levels decreased to <200 mg/dL with a concomitant increase of D-dimers in 1 patient only (Major Resection group). The median duration of epidural analgesia was 3 days. Because of disturbances in the coagulation profile, epidural catheters were left indwelling for 7 days in 6 patients (9%) (Major Resection group). No patients developed signs or symptoms of spinal hematoma.

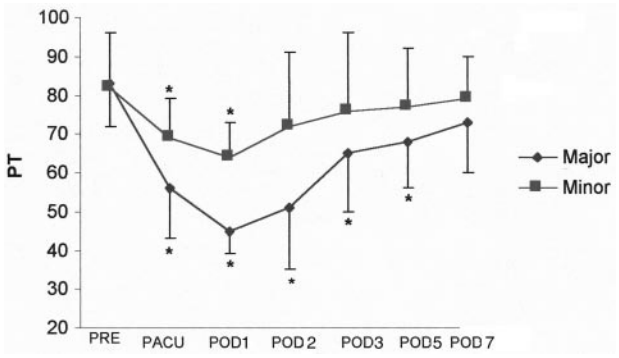

Figure 1. Changes in postoperative prothrombin time (PT) in patients undergoing major or minor liver resections. Values were expressed as mean ± SD. PRE = preoperative, PACU = postoperative anesthesia care unit, POD = postoperative day. *$P < 0.05$ compared with preoperative value.

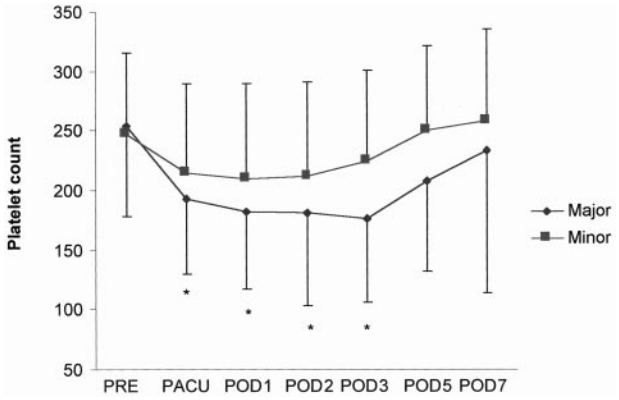

Figure 2. Changes in postoperative platelet count ($\times 10^3/mm^3$) in patients undergoing major or minor liver resections. Values were expressed as mean ± SD. PRE = preoperative, PACU = postoperative anesthesia care unit, POD = postoperative day. *$P < 0.05$ compared with preoperative value.

Discussion

The use of an indwelling epidural catheter and the timing of its removal in patients undergoing liver resection remain controversial and largely unstudied. Because of changes in the coagulation profile in the postoperative period (2,3), the use of epidural analgesia for these patients has been limited because of a theoretically increased risk of spinal hematoma (5). Previous studies have documented the relative safety of neuraxial blockade with subsequent anticoagulant therapy (6); however, unlike the coagulopathy associated with anticoagulant therapy, the hemostatic abnormalities associated with liver resection are not always predictable and/or reversible. In the present study of 136 patients undergoing uncomplicated liver resection, significant disturbances in PT were observed. However, in contrast to patients who underwent minor liver resection in whom PT returned to control value within 1 day, in patients undergoing major liver resection, the disturbances in PT were profound and prolonged, and a return to the preoperative value was achieved only at Day 5. Moreover, a decrease in platelet count was also observed in this group of patients. As a result, the epidural catheter could not be removed before POD 7 in 6 patients. In two of these patients, fresh frozen plasma was administered to normalize the coagulation profile before catheter removal.

Our study extends previous retrospective work that demonstrated in 24 patients undergoing living-related liver donor surgery, postoperative prolongation of the

PT which continued for 3–6 days (7,8). No epidural complications were reported in these patients. In another study that described the anesthetic management of living liver donors, the authors reported that epidural analgesia was the most commonly adopted mode of pain relief; however, there were no data regarding the clotting profile in the perioperative period (9). The report by Rees et al. (1), which examined the surgical technique of liver surgery, included a retrospective review of 150 resections performed under combined epidural-general anesthesia. The coagulation status and the time of catheter removal were not described in that study. Others have used patient-controlled analgesia to provide postoperative analgesia in patients undergoing living-related liver donor surgery because "the possibility the surgery would adversely affect postoperative coagulation and risk development of epidural hematoma" (10). The present study demonstrates the relative safety of continuous epidural analgesia in patients undergoing liver resection. However, because of the rarity of spinal hematoma, it is difficult to assess the relative risk of this complication in patients undergoing liver resection with an indwelling epidural catheter. For a sample size of 136 patients, the maximal incidence of epidural hematoma (with 95% confidence) is 2.2%. Also, in this study, we included only patients who did not require a perioperative transfusion of blood or blood products. This careful patient selection may have contributed to the zero incidence of adverse outcome.

In summary, the decision to insert an epidural catheter in patients undergoing hepatic resection should be made with care. Because the changes in coagulation in patients undergoing minor liver resection are brief, pain relief may be provided with epidural analgesia. However, in patients undergoing uncomplicated major hepatic resection, we must consider the possibility of a delay in epidural catheter removal or the need to administer fresh frozen plasma before catheter removal because of protracted coagulopathy. The PT and platelet count should be closely monitored postoperatively and before catheter removal, and all patients should be observed daily for early signs of cord compression. Although no sequelae of spinal hematoma with epidural catheters were observed, further study in large-scale trials that assess the safety of epidural catheters in this patient population is needed. Moreover, because the potential benefits of epidural analgesia for liver resection are undefined given the current available data, additional prospective randomized studies that compare the effectiveness and safety of IV or epidural analgesia in this patient population should be performed.

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