Epidural Bupivacaine–Morphine Analgesia versus *Patient-controlled Analgesia following Abdominal Aortic Surgery*

Analgesic, Respiratory, and Myocardial Effects

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Background: **The efficacy and effects of epidural analgesia compared with patient-controlled analgesia (PCA) have not been reported in patients undergoing major vascular surgery. We compared the effects of epidural bupivacaine-morphine with those of intravenous PCA morphine after elective infrarenal aortic surgery.**

Methods: **Forty patients classified as American Society of Anesthesiologists physical status 2 or 3 received general anesthesia plus postoperative PCA using morphine sulfate (group PCA; n = 21) or general anesthesia plus perioperative epidural morphine–bupivacaine (group EPI; n = 19) during a period of 48 h. During operation, EPI patients received 0.05 mg/kg epidural morphine and 5 ml 0.25% bupivacaine followed by an infusion of 0.125% bupivacaine with 0.1% morphine (0.1 mg/ml); group PCA received 0.1 mg/kg intravenous morphine sulfate. Continuous electrocardiographic monitoring (V4 and V5 leads) was performed from the night before surgery until 48 h afterward. Respiratory inductive plethysmographic data were recorded after tracheal extubation. Visual analog pain scores at rest and after movement were performed every 4 h after extubation.**

Results: **Nurse-administered intravenous morphine and time to tracheal extubation were less in group EPI, as were visual analog pain scores at rest and after movement from 20 to 48 h. Complications and the duration of intensive care unit and hospital stay were comparable. There was a similar, low incidence of postoperative apneas, slow respiratory rates, desaturation, and S-T segment depression.**

Conclusions: **Epidural morphine–bupivacaine is associated with reduced early postoperative intravenous opioid requirements, more rapid tracheal extubation, and superior analgesia after abdominal aortic surgery, with comparable respiratory effects. (Key words: Apneas; continuous monitoring; epidural local anesthetics; epidural opioids; outcome.)**

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BOTH systemic intravenous opioids and epidural analgesia using opioids either alone or in combination with local anesthetic agents provide good-quality analgesia after major surgery, but little comparative data exists on their efficacy and adverse effects in high-risk patients. Epidural opioids have a significant incidence of respiratory depression after major surgery, and their risk–benefit relationship is not clear.[1] Patient-controlled analgesia (PCA) has emerged as the standard technique for which no contraindications exist, but adverse respiratory effects have been reported, especially in elderly patients.[2] Epidural opioid–local anesthetic combination analgesia

may provide superior analgesia to epidural opioids given alone,[3] but the respiratory effects of such combinations have not been described.

The primary aims of this study were to compare the efficacy and respiratory effects of perioperative epidural administration of morphine–bupivacaine relative to a standard regimen of intravenous nurse-administered morphine, followed by intravenous PCA morphine. The effects of both analgesic regimens on respiratory function were compared using respiratory inductance plethysmography and pulse oximetry. A secondary aim was to investigate the daily incidence of S-T segment depression and its relationship to analgesic technique.

Materials and Methods

Patient Selection

The study protocol was approved by The Toronto Hospital Committee for Research on Human Subjects. Forty patients classified as American Society of Anesthesiologists physical status 2 and 3 who were undergoing elective infrarenal aortic aneurysm repair or aortobifemoral bypass grafting gave written informed consent to participate. Exclusion criteria included coagulopathy or anticoagulant therapy precluding randomization to epidural analgesia; preoperative chronic analgesic use or substance dependence; previous adverse reactions (other than nausea) to narcotic analgesics; and documented cerebrovascular disease or other neuropsychiatric illness, including a history of postoperative confusion. Patients with preoperative left bundle-branch block, cardiac glycoside use, or those with indwelling pacemakers were excluded from S-T segment monitoring.

Patient Allocation

Because we were precluded ethically from epidural placebo administration in patients scheduled for intraoperative heparinization, the study followed a randomized open design. After recruitment, patients received instruction in visual analog score (VAS) pain assessment and were randomly assigned to receive analgesia *via* (1) intraoperative and postoperative nurse-administered epidural morphine–bupivacaine (group EPI) or (2) intraoperative morphine sulfate, followed by nurse-administered morphine sulfate and then PCA morphine (group PCA).

Preoperative Management and Anesthesia

Beginning the evening before surgery, eligible patients underwent continuous S-T segment recording with a clinically validated[4,5] real-time S-T trend monitor (Monitor One; Q-Med Inc., Milwaukee, WI), with modified bipolar V4 and V5 chest leads placed as previously described.[6] S-T depression was defined as horizontal or downsloping S-T segment depression of 1 mm or more extending at least 60 ms beyond the J-point and lasting >60 s. Hard copy records of S-T depression were verified by an investigator (D.C.H.C.) who was blinded to the anesthetic technique.

Patients received premedication with 1 or 2 mg sublingual lorazepam 2 h before surgery together with routine prescription medications as appropriate. Before induction of anesthesia in patients in group EPI, an epidural catheter was placed at the L2–L3 or L3–L4 interspace, and a 3-ml dose of 2% lidocaine plus 1/200,000 epinephrine was injected. An additional 7 ml of 2% lidocaine was injected over 20 min. Anesthesia was induced in all patients with fentanyl (10–15 μg/kg) and sodium thiopental (1 or 2 mg/kg) and maintained using isoflurane, nitrous oxide, and oxygen. After tracheal intubation, patients in group EPI received 10 ml 0.25% bupivacaine over 20 min. After aortic unclamping and hemodynamic stabilization, EPI patients received 0.05 mg/kg epidural morphine and 5 ml 0.25% bupivacaine, whereas PCA patients received 0.1 mg/kg intravenous morphine sulfate. An epidural infusion of 0.1 mg/ml preservative-free morphine, and 0.125% bupivacaine was begun at 4 ml/h in all EPI patients. At completion of surgery, neuromuscular blockade was reversed with neostigmine-glycopyrrolate, and patients were transferred, with endotracheal tubes in place, to the surgical intensive care unit (SICU), as was routine practice when this study was performed.

Postoperative Monitoring

After patients were admitted to the SICU, mechanical ventilatory support was continued until their temperatures were normal and they were hemodynamically stable, awake, cooperative, and able to generate an adequate vital capacity and negative inspiratory force. Nurse-administered morphine sulfate was permitted in both groups for early postoperative analgesia. A four-point, patient-rated, numeric rating scale was used to assess pain while patients were still mechanically ventilated (0 = no pain, 1 = mild pain, 2 = moderate pain, 3 = severe pain). Sedation was scored by an experienced observer using a six-point scale[7] at hourly intervals until tracheal extubation. The sedation scale consisted of the following scores: 1 = patient anxious and agitated or restless or both; 2 = patient cooperative,

oriented, and tranquil; 3 = patient responds to commands only; 4 = patient responds briskly to a light glabellar tap or loud auditory stimulus; 5 = patient responds sluggishly to a light glabellar tap or loud auditory stimulus; 6 = patient does not respond at all to a light glabellar tap or loud auditory stimulus.

Decisions concerning weaning from ventilation were made by SICU staff uninvolved in the study, guided by the unit protocol.

After tracheal extubation, pain was assessed using a 10-cm VAS with 0 and 10 labeled as "no pain" and "worst pain imaginable," respectively.[8] The VAS scores were obtained at four hourly intervals at rest (VAS-R) and on movement (VAS-M) until 48 h after admission to the SICU. In group EPI, epidural bupivacaine–morphine infusions (0.125% bupivacaine, 0.1 mg/ml morphine) were continued at 4 ml/h and adjusted in response to patient status. Inadequate analgesia (VAS-R >4) was treated by a 5-ml bolus of epidural 0.25% bupivacaine and 0.05 mg/kg morphine followed by an increase in the infusion rate by an increment of 2 ml/h. To minimize unnecessarily high dosages, sustained low pain scores (VAS-M ≤3 for 4 h) mandated a decrease in the infusion rate by 2 ml/h to a minimum of 4 ml/h. Patients in group PCA received nurse-administered morphine sulfate for analgesia until they were deemed able to use a PCA infusion device (Life Care II Infuser, Abbott, Chicago, IL) programmed to deliver intravenous morphine sulfate (1-mg bolus), with a 6-min lock-out period, a 4-h maximum dose of 30 mg, and with no continuous background infusion. No other analgesic agents were used.

Postoperative Assessment

Immediately after tracheal extubation, respiratory monitoring was begun using respiratory inductance plethysmography (NIMS, Miami Beach, FL) and pulse oximetry (model N-100; Nellcor, Hayward, CA). After a setup and calibration procedure,[9] the average respiratory rate was recorded continuously in 5-min epochs, and episodes of apnea (15-s intervals with no tidal volume >100 ml) and slow respiratory rate (any 5-min interval with an average respiratory rate <10 breaths/min) were recorded. All episodes of oxygen saturation <90% were noted.

Patients were monitored continuously for 48 h by a trained research observer who verified data and revalidated respiratory inductance plethysmography function when necessary. Adverse effects (pruritus, nausea, motor blockade) were recorded if present. All patients had indwelling urinary catheters for the duration of the study.

Withdrawal of Patients from the Study

Withdrawal criteria included (1) failure of surgery to proceed as planned and (2) development of postoperative complications limiting assessment. In cases of withdrawal, data collected up to the time of discontinuation were retained for analysis.

Statistical Analysis

Before the study was begun, a sample size calculation was performed. Based on anticipated control (PCA) VAS-M scores of 6 ± 2.5 (mean ± SD), we calculated a sample size such that a between-group mean difference in postoperative VAS-M of 2, with reduced pain scores in group EPI, would (1) permit a type 1 error rate of one-tailed $\alpha = 0.05$, and (2) under the alternate hypothesis retain the null hypothesis with a type 2 error of $\beta = 0.20$ (*i.e.*, power equal to 0.80). Therefore we estimated that a total sample size of 40 patients would be required.

Demographic data were analyzed using one-way analysis of variance or Fisher's exact test as appropriate. Sedation scores, numeric rating scale pain scores, and nurse-administered morphine during ventilation were compared between the groups using the Mann-Whitney U test. The Bonferroni type 1 error rate adjustment (alpha/number of tests) was used to correct for multiple tests of significance. The VAS pain scores were analyzed by three-way analysis of variance, with group as the between-group factor and pain type (VAS-R, VAS-M) and time after surgery as the two repeated-measures factors. Respiratory variables were analyzed by two-way analysis of variance, with group as the between-group factor and time after surgery as the repeated measures factor. Significant interaction effects were analyzed by simple main effects using a pooled mean square error and Satterthwaite's adjusted degrees of freedom.[10] Continuous data are presented as mean ± SD or median ± interquartile range (Q1–Q3) as appropriate; categorical data are presented as frequencies. Initial data analysis was by intention to treat for all variables. Statistical significance was inferred for $P \leq 0.05$.

Results

Demographic and Surgical Variables

Table 1 summarizes demographic and surgical data for the two groups (EPI = 19, PCA = 21). Treatment groups