European Journal of Anaesthesiology 2008; **25:** 763–780

Correspondence

Intraoperative epidural analgesia does not reduce time of postoperative analgesic treatment compared to intravenous analgesia

doi:10.1017/S0265021508004031

EDITOR:

Thoracic epidural analgesia (TEA) is an effective technique in major abdominal surgery, but in daily clinical routine there is still no consensus on whether it should be used intraoperatively or only postoperatively. One benefit of intraoperative use of TEA should be lower analgesic requirements [1], but the conclusions have been inconsistent [2,3]. This double-blind randomized study was designed to compare two strategies that are often used in clinical practice: combined vs. balanced anaesthesia. We focused on the length of postoperative patient-controlled epidural analgesia (PCEA), because PCEA is an expensive form of analgesic treatment with costs proportional to duration [4]. Our aim was to determine whether intraoperative TEA could reduce the time of postoperative epidural treatment.

Ethics Board approval was obtained, and all patients gave written informed consent. All patients scheduled for major abdominal surgery by laparotomy were screened. Inclusion criteria were age above 18 yr, ASA physical status I-III and knowing the German language. Exclusion criteria were contraindications to epidural analgesia or use of opioid analgesics during the past month. Patients were randomized to either intraoperative combined epidural/general anaesthesia (ICEA) or balanced anaesthesia (control, non-ICEA). Postoperatively both groups received PCEA.

All patients were administered midazolam 7.5 or 3.75 mg, according to weight and age, 45 min before transfer. Crystalloids were infused at 10 mL kg^{-1} over 15 min. Then all patients underwent thoracic epidural catheterization using the midline approach and loss-of-resistance technique. Spinal placement was excluded by aspiration and the injection of a test dose of 2–3 mL bupivacaine 0.5%. Infusion of crystalloids was continued at 10 mL kg^{-1} h^{-1}. General anaesthesia was induced in both groups with 3.0–5.0 mg kg^{-1} thiopental, 1.5–3.0 μg kg^{-1} fentanyl, 0.1–0.2 mg kg^{-1} *cis*-atracurium or 1.0–1.5 mg kg^{-1} succinylcholine.

The ICEA group received a 6–8 mL epidural bolus of sufentanil 1 μg mL^{-1} and ropivacaine 0.16%, 30 min pre-incision. Anaesthesia and analgesia were maintained with isoflurane in oxygen/air and continuous epidural infusion of sufentanil 1 μg mL^{-1} and ropivacaine 0.16% at 6 mL h^{-1}. If necessary, additional epidural boluses of sufentanil/ropivacaine were administered or the rate of the epidural infusion was modified, to maintain a bispectral index (BIS) of 40–50 and clinical signs of sufficient anaesthesia.

The control group received a combination of isoflurane in oxygen/air and fentanyl intravenously (i.v.). Shortly before the skin incision, 4–6 μg kg^{-1} fentanyl was injected. During surgery, fentanyl injection was repeated as necessary to achieve a BIS of 40–50 and clinical signs of sufficient anaesthesia. TEA was started with an 8 mL bolus of 1 μg mL^{-1} sufentanil in ropivacaine 0.16% at the closure of the abdomen. A continuous epidural infusion of the same sufentanil/ropivacaine solution was started immediately at 6 mL h^{-1}.

Postoperatively, both groups received continuous TEA (sufentanil 1 μg mL^{-1} and ropivacaine 0.16%), starting with 6 mL h^{-1}. Additional patient-controlled analgesia via bolus was possible (4 mL bolus, 20 min lockout). The block was tested and documented immediately after the patients awoke. The 24 h sufentanil/ropivacaine requirement, additional analgesic demand and complications of epidural analgesia were documented twice daily thereafter by staff blinded to the patients' study assignments. Pain was evaluated every 4 h on a 0–100 numeric rating scale (NRS). A protocol algorithm was used for reducing the flow rate of epidural analgesics and for termination of postoperative PCEA.

Correspondence to: Erika Schulte, Klinik für Anästhesiologie und operative Intensivmedizin, Charité, Campus Virchow Klinikum, Universitätsmedizin Berlin, Augustenburger Platz 1, D-13353 Berlin, Germany. E-mail: erika.schulte@charite.de; Tel: +49 30 450 551001; Fax: +49 30 450 551909

Accepted for publication 5 March 2008 EJA 4656
First published online 10 April 2008

It was calculated that 46 patients would be needed in each group, to detect a 1-day reduction in PCEA treatment duration, at a power of 80% and $P < 0.05$. The data were analysed by χ^2-test, paired two-tailed *t*-tests, Mann–Whitney rank sum test, Kaplan–Meier technique and log rank test. The analysis was undertaken using SPSS 12.0 (SPSS Inc., Chicago, IL, USA).

We screened 229 consecutive patients, recruited 136 subjects and had 95 complete datasets available (53 controls and 42 ICEA). The two groups did not differ significantly in patient characteristics, ASA classification, pre-existing medical conditions, diagnoses or surgical procedures. There was no difference in duration of surgery (mean 4 h), end-tidal isoflurane concentration at any time, extubation time, fluid intake, fluid loss or mean arterial pressure. The desired BIS of 40–50 was maintained during anaesthesia in both groups. The control group needed a mean of 0.75 mg ($2.8\ \mu g\ kg^{-1}\ h^{-1}$) i.v. fentanyl during surgery, whereas the ICEA group needed a mean of 39 μg sufentanil epidurally ($0.13\ \mu g\ kg^{-1}\ h^{-1}$) but no fentanyl.

Intraoperative epidural analgesia did not reduce the duration of postoperative pain treatment compared to balanced anaesthesia with i.v. opioid. The PCEA was stopped after 5 days on average, independent of whether TEA was started early, intraoperatively or postoperatively. The epidural analgesic consumption and supplemental analgesic requirements were identical in both groups. There were no significant differences in any of the four measures of dosage of sufentanil and ropivacaine: total (Fig. 1), basal, additional patient-initiated boluses or doctor-initiated additional boluses. Additional analgesia using another route such as oral or i.v. was necessary only in about 10% of the patients, independent of the study group. The pain intensity was comparably low in both groups. About two-thirds of the patients had no pain most of the day, regardless of whether it was the first or last day of PCEA treatment.

A possible explanation as to why intraoperative TEA was no better than postoperative TEA is that the control group received entirely sufficient intraoperative analgesia. Fentanyl was i.v. administered in our study at the high dosage of $2.8\ \mu g\ kg^{-1}\ h^{-1}$. Our results are consistent with those of Burmeister and colleagues [5], who used $37\ \mu g\ kg^{-1}\ h^{-1}$ sufentanil, thus an equianalgesic dose of $3.7\ \mu g\ kg^{-1}\ h^{-1}$ fentanyl [6]. By contrast, Katz and colleagues applied only about $1.5\ \mu g\ kg^{-1}\ h^{-1}$ fentanyl in the control group and found that they did not do as well as the experimental group [1]. Most other studies have not reported the opioids used in the control group.

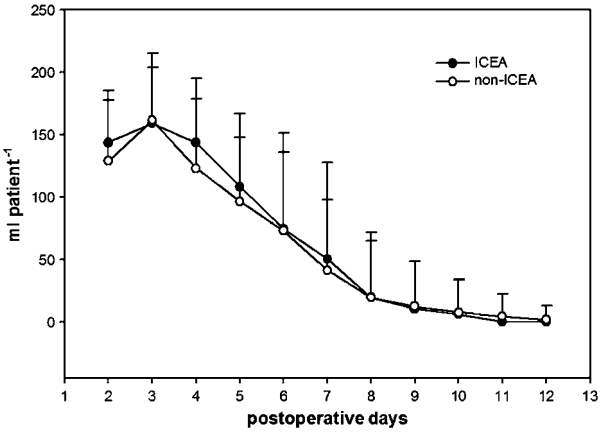

Figure 1.
Postoperative daily epidural sufentanil and ropivacaine requirement. Values are means + SD. There were no significant differences in these factors betweeen the two groups. ICEA: intraoperative combined epidural anaesthesia (intervention group); non-ICEA: control group with balanced anaesthesia.

There were no severe complications from the epidural technique. Pulmonary and abdominal complications occurred, but there were no advantages for either group. There was no significant difference in ICU duration (mean 1.5 days) or total hospital stay (mean 24 days).

The rate of nausea was 21% in non-ICEA patients vs. 7% in ICEA patients ($P = 0.06$), and the rate of vomiting was 8% vs. 2% ($P = 0.28$). Opioids are a risk factor for nausea and vomiting with a strong dose–response relationship [7]. It may be assumed that the equianalgesic dose ratio between the two study groups is 10 : 1 [6]. Comparing the equianalgesic doses (ICEA 39 μg vs. non-ICEA 75 μg sufentanil for the entire surgery time), the opioid dosage of the ICEA group seems to have been lower, perhaps due to effect of the local epidural anaesthetic.

In conclusion, TEA did not reduce the duration of postoperative PCEA treatment, extubation time, complication rates, readmissions, ICU stay or hospitalization time. The most plausible explanation is that the control group received entirely adequate analgesia, which could not be improved by intraoperative TEA. At least on the basis of our results, there does not appear to be any reason to prefer intraoperative TEA or i.v. opioids, so long as the patient receives sufficient analgesia.

E. Schulte, B. Hoffmann, C. Höhne, M. Hofmann, W. Olenberger, G. A. Fritz
Department of Anesthesiology and Intensive Care Medicine
Charité University Hospital
Berlin, Germany

Acknowledgements

The authors would like to thank all their colleagues, the nursing staff, the Acute Pain Service members and Güven Braune, for their participation in conducting the study. The authors would also like to thank Michael Hanna, PhD, for editing the manuscript. This study was supported by a grant for C. Höhne from the B. Braun Foundation (Melsungen, Germany). The results of this study were presented in part at the 24th Congress of the European Society of Regional Anesthesia and Pain Therapy in Berlin, September 2005.

References

1. Katz J, Cohen L, Schmid R, Chan VWS, Wowk A. Postoperative morphin use and hyperalgesia are reduced by preoperative but not intraoperative epidural analgesia. *Anesthesiology* 2003; **98**: 1449–1460.
2. Moiniche S, Kehlet H, Dahl JB. A qualitative and quantitative systematic review of preemptive analgesia for postoperative pain relief. *Anesthesiology* 2002; **96**: 725–741.
3. Ong CK, Lirk P, Seymour RA, Jenkins BJ. The efficacy of preemptive analgesia for acute postoperative pain management: a meta-analysis. *Anesth Analg* 2005; **100**: 757–773.
4. Bartha E, Carlsson P, Kalman S. Evaluation of costs and effects of epidural analgesia and patient-controlled intravenous analgesia after major abdominal surgery. *Br J Anaesth* 2005; **96**: 111–117.
5. Burmeister MA, Gottschalk A, Freitag M *et al*. Pre- and intraoperative epidural ropivacaine have no early preemptive analgesic effect in major gynecological tumour surgery. *Can J Anaesth* 2003; **50**: 568–573.
6. Cherny NI. Opioid analgesics: comparative features and prescribing guidelines. *Drugs* 1996; **51**: 713–737.
7. Roberts GW, Bekker TB, Carlsen HH, Moffatt CH, Slattery PJ, McClure AF. Postoperative nausea and vomiting are strongly influenced by postoperative opioid use in a dose-related manner. *Anesth Analg* 2005; **101**: 1343–1348.

A rare cause of maternal death: liver and inferior vena cava rupture due to previously undiagnosed Ehlers-Danlos Syndrome type IV

doi:10.1017/S0265021508004006

EDITOR:
A 23-yr-old primigravid female died 8 days post Caesarean section due to liver decapsulation and inferior vena cava rupture due to previously undiagnosed Ehlers-Danlos Syndrome type IV (EDS IV). Her past medical history included many features suggestive of a connective tissue disorder but the diagnosis was only made *post mortem*.

Case report

The patient was a 23-yr-old primigravid female. Her booking summary documented an operation for 'protruding eyes' and that her 18-yr-old brother had previously had a heart transplant.

She was admitted at term for induction of labour for intrauterine growth retardation. An epidural was sited and after an 8 h labour a Caesarean section was performed for fetal distress. The epidural was topped up and anaesthesia deemed adequate. However, 5 min into the procedure she was given a general anaesthetic as she was experiencing pain. A healthy female baby was delivered. There was 700 mL blood loss and tissue friability was noted. The possibility of a collagen disorder was raised. Postoperative recovery was uneventful and she was discharged home 3 days later.

The patient was readmitted 5 days post-operatively with dull chest pain and shortness of breath on exertion. Arterial blood gas analysis revealed a mild respiratory alkalosis with a normal PaO_2 on air. Dalteparin was commenced for a presumptive diagnosis of pulmonary embolus. She then developed sharp right shoulder pain and signs of respiratory distress with hypoxia and tachypnoea. The admission blood results were documented at this stage, haemoglobin 10.6 g dL^{-1} and elevated serum transaminases, bilirubin and alkaline phosphatase. The obstetric registrar noted an increasing abdominal girth but a portable ultrasound scan revealed no ascites. The differential diagnoses of HELLP syndrome and acute fatty liver of pregnancy were discussed with the regional liver

Correspondence to: Andrew D. Combeer, Department of Anaesthesia, Royal Surrey County Hospital, Egerton Road, Guildford, Surrey, GU2 7XX, UK. E-mail: combeer@doctors.org.uk; Tel: +44 1483 464116; Fax: +44 1483 453135

Accepted for publication 22 February 2008 EJA 4984
First published online 10 April 2008