Efficacy of Postoperative Epidural Analgesia
A Meta-analysis

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Awareness of the under-treatment of acute pain, introduction of new pain management standards by the Joint Commission on Accreditation of Healthcare Organizations (JCAHO), and recognition of the untoward consequences of uncontrolled postoperative pain have led to a greater appreciation for the importance of acute postoperative pain control. Inadequate control of postoperative pain may result in a higher incidence of chronic postsurgical pain, and worsened patient-oriented outcomes such as quality of life.

More than 40 million inpatient surgical procedures were performed in the United States in 2000, with systemic opioids (frequently administered parenterally) and epidural analgesia used probably as the 2 most common forms of postoperative analgesia. However, delivery of medications, especially local anesthetic drugs, directly into the epidural space (epidural analgesia) may provide better pain control and improve perioperative pathophysiology, resulting in decreased postoperative morbidity.

The question of whether epidural analgesia provides better pain control than parenteral opioid analgesia has not been examined in a systematic fashion, despite the analgesic benefits demonstrated in some individual randomized controlled trials (RCTs). Most studies have focused on whether epidural therapy improves traditional anesthetic outcomes, such as myocardial ischemia, myocardial infarction, or death, and not on analgesia. It is not clearly established whether postoperative epidural analgesia is better than systemic opioids or if the adverse effect profiles differ. In addition, epidural analgesia should not be considered as a single generic entity because many factors (eg, the congruency of catheter insertion location to site of surgical incision [catheter-incision congruency], type of analgesic regimen [local anesthetic vs opioid], and type of pain

Context Whether epidural analgesia is a better method than parenteral opioids for postoperative pain control remains controversial.

Objective To systematically review the efficacy of postoperative epidural analgesia vs parenteral opioids, the primary alternative technique.

Data Sources Studies were identified primarily by searching the National Library of Medicine’s PubMed database (1966 to April 25, 2002) and other sources for studies related to postoperative epidural analgesia.

Study Selection Inclusion criteria were a comparison of epidural therapy vs parenteral opioids for postoperative analgesia, measurement of pain using a visual analog scale (VAS) or numeric rating scale, randomization of patients to either therapy, and adult patients (≥18 years). A total of 1404 abstracts were identified, 100 of which met all inclusion criteria.

Data Extraction Each article was reviewed and data extracted from tables, text, or extrapolated from figures as needed. Weighted mean pain scores, weighted mean differences in pain score, and weighted incidences of complications were determined by using a fixed-effect model.

Data Synthesis Epidural analgesia provided better postoperative analgesia compared with parenteral opioids (mean [SE], 19.40 mm [0.17] vs 29.40 mm [0.20] on the VAS; P<.001). When analyzed by postoperative day, epidural analgesia was better than parenteral opioids on each postoperative day (P<.001 for each day after surgery). For all types of surgery and pain assessments, all forms of epidural analgesia provided significantly better postoperative analgesia compared with parenteral opioid analgesia (P<.001 for all), with the exception of thoracic epidural analgesia vs opioids for rest pain after thoracic surgery (weighted mean difference, 0.6 mm; 95% confidence interval, –0.3 to 1.5 mm; P=.12). The complication rates were lower than expected for nausea or vomiting and pruritus but comparable with existing data for lower extremity motor block.

Conclusion Epidural analgesia, regardless of analgesic agent, location of catheter placement, and type and time of pain assessment, provided better postoperative analgesia compared with parenteral opioids.
Box. Categories of Data Analyzed From Each Study

**Methodology**
- Blinding: yes, no
- Region of surgery: thoracic, abdominal, pelvic, lower extremity, cesarean delivery, multiple

**Epidural Data**
- Epidural location: thoracic, lumbar
- Type of epidural infusion: opioid, local anesthetic, combination of local anesthetic and opioid

**Parenteral Opioid Data**
- Parenteral route: intravenous, including intravenous PCA*; subcutaneous; intramuscular

**Pain Scores on Postoperative Days 1-5, Converted to 0-100 Scale**
- Pain score: rest
- Pain score: incident (eg, coughing with activity)

**Major Complications (Incidence Rates)**
- Death
- Stroke
- Cardiovascular complications: hypotension, myocardial infarction, myocardial ischemia, arrhythmia
- Pulmonary complication: respiratory depression, incidence of desaturation events, pneumonia, other atelectasis
- Renal complications
- Deep venous thrombosis, pulmonary embolism

**Minor Complications (Incidence Rates)**
- Nausea or vomiting (whichever was more frequent)
- Confusion or delirium
- Sedation
- Pruritus
- Constipation
- Urinary retention
- Headache
- Backache
- Motor block/weakness

*PCA indicates patient-controlled analgesia.

assessment [rest vs dynamic]) may influence its efficacy.

We performed a meta-analysis of available RCTs that randomized patients receiving postoperative analgesia to either epidural analgesia or parenteral opioids. The analgesic efficacy of epidural analgesia was analyzed according to catheter-incision congruency, type of analgesic regimen, postoperative day, and type of pain assessed.

**METHODS**

**Literature Review**
The National Library of Medicine’s PubMed database was searched from 1966 to April 25, 2002, for all abstracts containing words related to epidural therapy (epidural, peridural, or extradural) combined with analgesia (pain or analgesia) and surgical procedures (operative, operation, surgery, or surgical), using the usual Boolean meanings of “or” and “and.” A total of 5595 articles were found. A second search was made by using the corresponding Medical Subject Headings (MeSH) terms ([anesthesia, epidural, analgesia, epidural, or injections, epidural] and pain, postoperative and surgical procedures, operative), which resulted in finding 849 abstracts. The 2 searches were combined by using the or term and limited to clinical trials and the English language, resulting in a total of 1404 articles.

Each of the 1404 abstracts after reviewing the full articles was then reviewed by 1 of the authors (B.M.B., A.R.C., C.L.W.) for inclusion in the meta-analysis. Only studies that compared postoperative epidural therapy vs parenteral opioid analgesia using visual analog scale (VAS) measurements of pain or a similar substitute (numerical rating scale) in a randomized fashion were included. Epidural analgesia was defined as medicine delivered into the epidural space by infusion, patient-controlled analgesic device, or by repeated bolus dosing. Studies in which a single epidural dose was given at the time of surgery were not included. Parenteral analgesia was defined as opioid drugs given by bolus dosing, infusion, or patient-controlled analgesic device via the intravenous, subcutaneous, or intramuscular routes.

No minimum sample sizes were required for inclusion of studies in the analysis. Only randomized studies with adults aged 18 years or older were included. Any disputes were resolved by agreement of at least 2 reviewers (B.M.B., C.L.W.). A total of 1304 articles were rejected for the following reasons: 738 were not comparisons of postoperative parenteral and epidural analgesia, 367 articles did not report measures of postoperative pain, 81 did not report VAS pain scores, and 118 involved patients younger than 18 years. After selecting the initial articles, the reference list of each analyzed article was checked for any additional studies, as were the author’s personal files, and no additional references that met all inclusion criteria were found.

**Data Extraction and Analysis**
The Box includes all analyzed items. Each study’s methodology and results were recorded, with data extrapolated from graphs as needed. Definition of complications was recorded as originally defined by the study and the incidence of that complication as reported by the study was recorded. For nausea and vomiting, the higher num...
ber was recorded if both were reported. In some studies, data could not be translated into an incidence rate (a histogram of pulse oximetry values over time) and those data were not entered into the database. However, we did incorporate the remainder of that study’s data as feasible.

All reported data were included as unique observations and subgrouped as described. The VAS or numerical rating scale pain scores were converted to a 0 to 100 scale. The VAS data were weighted by sample size, and if a given article measured pain at multiple time points, all measurements were included in the analysis. The number reported is the total number of patient observations (1 study of 10 patients that measured pain at 3 different time points would contribute the number 30 to the overall sample size). The global mean VAS (weighted for patient observations) and for each postoperative day up to 4 days after surgery between epidural analgesia and systemic opioids were compared. Epidural analgesia is not a generic entity because many factors (analogic regimen [local anesthetics vs opioids] and catheter-incision congruency) may influence the quality of postoperative analgesia. We subdivided the data by analgesic regimen and location/type of surgery and compared epidural to parietal techniques.

All epidural infusions containing local anesthetic were considered equivalent, including those with and without opioid. Similarly, all parenteral opioids were bundled (data from all the different parenteral opioids were combined). Both rest and incident pain were included in the analysis, analyzed separately, and again divided into subgroups depending on epidural location and infusion type. If an included study did not specify the neuraxial location of the epidural catheter, had a mix of epidural placements, or had multiple surgical sites, the article was not included in the subgroup analysis.

A fixed-effect model was used and the level of significance for all tests was set at an α level of .05 and variances were not assumed to be equal. A Kolmogorov-Smirnov test showed that the data were not normally distributed; instead, both epidural and parenteral opioid data were positively skewed. Because the data were not normally distributed, Mann-Whitney test was used to compare VAS pain scores between treatment groups. For complication data, an independent samples t test, weighted by sample size, was performed. Bonferroni correction was used for multiple comparisons of postoperative day VAS data. All other data analyzed were single comparisons between epidural and parenteral analgesia groups. All statistical analyses were performed with SPSS version 10.07 (SPSS Inc, Chicago, Ill). P<.05 was considered statistically significant.

After the data compilation was complete, further analyses were performed to assess the validity of the conclusions. We performed an analysis of the file drawer problem (how many unpublished studies or subjects showing no difference between treatment regimens would be needed to be discovered in someone’s file drawer to invalidate our results). By using techniques described by Rosenthal,12 we calculated the number of file drawer subjects needed to invalidate our results to be 94,273 subjects, an extremely high number of subjects for this type of trial. A funnel plot (Figure 1) was also created to determine the presence of publication and other biases (English language, citation, and multiple publication)13 in the meta-analysis. The funnel plot of the natural logarithm relative VAS (VAS in patients with epidural analgesia/VAS with parenteral opioids) vs trial precision (inverse of SD) was symmetric and centered around a relative VAS of less than 1.0, suggesting that there is no publication bias or other biases.13 Relative VAS was calculated for each trial by dividing the mean VAS from patients with epidural analgesia by the mean VAS from patients with parenteral analgesia.

RESULTS

Included Studies

A total of 100 articles met all inclusion criteria. Some of these articles used 2 or more treatment regimens, giving a total of 124 comparisons of epidural vs parenteral analgesic regimens. The characteristics of included studies, which also contain additional data (demographics and study location) recorded but not necessarily quantified for analysis, are shown in Table 1. A detailed table of included studies is available from the authors. Articles measured pain after a wide variety of operations and emanated from medical centers all over the world. Pain was measured after abdominal surgery in 45 studies (36%); thoracic (24%, n=30) and lower extremity (12%, n=15) surgery were the next most common types of surgery studied. Only 32% of the epidural patients (n=39 studies) received local anesthetic and opioid, although 53% received opioid alone with the choice of epidural opioid being predominantly morphine (40%) followed by fentanyl (21%). For parenteral opioids, morphine (40%) was most commonly used, followed by fentanyl (21%) and sufentanil (11%).

Forty-eight percent of studies used intravenous patient-controlled analgesia (PCA) as the delivery modality for par-
**POSTOPERATIVE EPIDURAL ANALGESIA**

Table 1. Characteristics of Included Studies (N = 124)*

<table>
<thead>
<tr>
<th>Study location</th>
<th>Abdominal</th>
<th>Thoracic</th>
<th>Lower extremity</th>
<th>Cesarean delivery</th>
<th>Pelvic</th>
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</tr>
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<td></td>
</tr>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
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<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
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<td></td>
<td></td>
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Study population, sex

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<tr>
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<th>Women</th>
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</thead>
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<tr>
<td>79 (64)</td>
<td>7 (6)</td>
<td>26 (21)</td>
</tr>
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</table>

Study location

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<th>Europe</th>
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<th>Canada</th>
<th>Asia/Australia</th>
<th>Multiple</th>
</tr>
</thead>
<tbody>
<tr>
<td>63 (51)</td>
<td>25 (20)</td>
<td>20 (16)</td>
<td>14 (11)</td>
<td>2 (2)</td>
</tr>
</tbody>
</table>

Table 2 compares the analgesia achieved by epidural and parenteral techniques subdivided by surgical site, catheter placement, and infusion type. For thoracic surgery, all epidural regimens provided significantly better postoperative analgesia compared with parenteral opioid (P < .001) (TABLE 3). A notable exception was with the use of TEA with opioid for rest pain after thoracic surgery, which produced an equivalent result (weighted mean difference in VAS, 0.6 mm; 95% CI, 0.4-5.3 mm; P = .12).

Rest vs Incident Pain

Many patients can achieve analgesia at rest, but not with movement, with parenteral opioids. Nearly all epidural regimens provided better postoperative pain control compared with parenteral opioids for both rest and incident pain (P < .001) (TABLE 3). A notable exception was with the use of TEA with opioid for rest pain after thoracic surgery, which produced an equivalent result (weighted mean difference in VAS, 0.6 mm; 95% CI, 0.4-5.3 mm; P = .12).

For thoracic surgery, TEA with local anesthetic with or without opioid receiving TEA with local anesthetic with or without opioid. The weighted mean difference in VAS (positive numbers favor epidural analgesia) was better with TEA with local anesthetic with or without opioid group was 11.2 mm (95% CI, 9.9-12.5 mm), although the weighted mean difference in VAS for LEA with opioid and TEA with opioid groups were 4.2 mm (95% CI, 2.2-6.2 mm) and 2.9 mm (95% CI, 0.4-5.3 mm), respectively.

For abdominal surgery, all epidural regimens were better than parenteral opioids (P < .001). The largest weighted mean difference in VAS was with local anesthetic with or without opioid either through TEA (10.9 mm; 95% CI, 10.1-11.6 mm) or LEA (17.8 mm; 95% CI, 15.8-19.9 mm). For pelvic surgery, including cesarean deliveries, all 3 epidural regimens provided significantly better analgesia compared with parenteral opioids (LEA with local anesthetic with or without opioid: weighted mean difference in VAS, 7.2 mm; 95% CI, 5.8-8.6 mm; LEA with opioid: 8.6 mm; 95% CI, 7.2-10.1 mm; TEA with local anesthetic with or without opioid: 10.5 mm; 95% CI, 7.1-14.0 mm; P < .001 for all). For lower extremity surgery, LEA with local anesthetic with or without opioid and LEA with opioid alone were both better than parenteral opioid (12.6 mm; 95% CI, 10.1-15.0 mm and 9.4 mm; 95% CI, 6.8-11.9 mm, respectively; P < .001 for both). No trials using TEA for lower extremity surgery were uncovered by this investigation.

Enteral opioid. When weighted by each study’s sample size, parenteral morphine was most commonly used (41.4% of patient-observations), followed by fentanyl (31.0%), sufentanil (7.5%), hydromorphone (1.7%), meperidine (1.5%), alfentanil (0.5%), and buprenorphine (0.5%), although 15.7% of patient-observations did not specify the opioid used or used a different opioid. Some articles were not included in the subgroup analysis because they did not specify the neuraxial location of the epidural catheter (16 articles), had a mix of epidural placements (8 articles), or had multiple surgical sites (6 articles).

**Pain**

When all studies and observations were combined, epidural analgesia provided better postoperative analgesia compared with parenteral opioids (P < .001). The weighted mean difference (SEM) in analgesia was 10.0 mm better (29.40 mm [0.20 mm] for opioid analgesia vs 19.40 mm [0.17 mm] for epidural analgesia) on the VAS scale for epidural analgesia (95% confidence interval [CI], 9.5-10.5 mm). The quality of analgesia may be different at different points in the postoperative recovery period, so pain scores were also assessed at different postoperative times (FIGURE 2). All observations made during a given postoperative day were included as unique data points. Epidural analgesia was better than parenteral opioid analgesia at all time points (P < .001 for each day after surgery). Analgesia may differ between parenteral regimens; however, when all trials were compiled, we found no difference in mean VAS between intravenous PCA and intramuscular or subcutaneous opioid administration. Intravenous PCA is commonly thought to be the standard of care for parenteral opioid administration. When compared with intravenous PCA alone, epidural analgesia provided a significantly better analgesia with lower overall mean VAS and mean VAS on each postoperative day.

Abbreviation: PCA, patient-controlled analgesia.

*Refers to none specified in the article.

**TABLE 2**

<table>
<thead>
<tr>
<th>Infusion</th>
<th>Site</th>
<th>Opioid</th>
<th>Parenteral opioids Method of administration</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lumbar</td>
<td>Morphine Fentanyl</td>
<td>Intravenous PCA</td>
</tr>
<tr>
<td></td>
<td>Thoracic</td>
<td>Sufentanil</td>
<td>As needed</td>
</tr>
<tr>
<td></td>
<td>Lower extremity</td>
<td>Other</td>
<td>Bolus</td>
</tr>
<tr>
<td></td>
<td>Cesarean delivery</td>
<td>None</td>
<td>Infusion</td>
</tr>
<tr>
<td></td>
<td>Pelvic</td>
<td>Local anesthetic with opioid</td>
<td>60 (48)</td>
</tr>
<tr>
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<td>Spine</td>
<td>Local anesthetic</td>
<td>52 (42)</td>
</tr>
<tr>
<td></td>
<td>Multiple</td>
<td>Morphine</td>
<td>16 (13)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fentanyl</td>
<td>19 (15)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sufentanil</td>
<td>7 (6)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Other</td>
<td>6 (5)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>None</td>
<td>3 (2)</td>
</tr>
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</table>

FIGURE 2. Table 2 compares the analgesia achieved by epidural and parenteral techniques subdivided by surgical site, catheter placement, and infusion type. For thoracic surgery, all epidural regimens provided significantly better postoperative analgesia compared with parenteral opioid analgesia (P < .001 for thoracic epidural analgesia [TEA] with local anesthetic with or without opioid; P = .002 for TEA with opioid alone; P < .001 for lumbar epidural analgesia [LEA] with opioid alone). The largest improvement in analgesia was observed in those patients receiving TEA with local anesthetic with or without opioid. The weighted mean difference in VAS (positive numbers favor epidural analgesia) with TEA with local anesthetic with or without opioid group was 11.2 mm (95% CI, 9.9-12.5 mm), although the weighted mean difference in VAS for LEA with opioid and TEA with opioid groups were 4.2 mm (95% CI, 2.2-6.2 mm) and 2.9 mm (95% CI, 0.4-5.3 mm), respectively.

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For thoracic surgery, TEA with local anesthetic with or without opioid...
yielded a similar improvement for both rest and incident pain with a weighted mean difference in VAS of 10.7 mm (95% CI, 9.3-12.0 mm) and 11.5 mm (95% CI, 9.4-13.6 mm), respectively, although TEA with opioid significantly improved incident pain by 5.9 mm (95% CI, 3.6-8.2 mm) but did not improve control of rest pain (0.6 mm; 95% CI, –0.3 to 1.5 mm). Compared with parenteral opioid for abdominal surgery, local anesthetic with or without opioid via TEA or LEA quantitatively appeared to provide larger improvements in VAS than epidural opioids alone (weighted mean difference in VAS: TEA with local anesthetic with or without opioid at incident: 6.3 mm; 95% CI, 5.4-7.1 mm; LEA with opioid at rest: 5.8 mm; 95% CI, 4.4-7.1 mm). Only LEA was used in lower extremity surgery. The decrease in incident pain with local anesthetic with or without opioid was significant with a weighted mean difference in VAS of 34.6 mm (95% CI, 28.9-40.3 mm). Otherwise, the decrease in pain was similar across regimens (LEA with local anesthetic with or without opioid at rest: 4.8 mm; 95% CI, 2.7-6.9 mm; LEA with opioid at rest: 9.4 mm; 95% CI, 6.8-11.9 mm).

Effect of Nonblinded Trials

Of the 100 included trials, only 44 incorporating 55 comparisons were blinded (data available from author). Studies on pain may be influenced by the placebo effect41; therefore, we confirmed the main results of the meta-analysis by using only the blinded trials. The overall VAS and improvement in

<table>
<thead>
<tr>
<th>Surgical Site</th>
<th>Epidural Location</th>
<th>Epidural Infusion</th>
<th>No. of Studies</th>
<th>No. of Observations</th>
<th>Parenteral Mean VAS (SEM), mm</th>
<th>Epidural Mean VAS (SEM), mm</th>
<th>Weighted Mean Difference (95% CI), mm</th>
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<td>Opioid alone</td>
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<td>24.7 (0.9)</td>
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<td></td>
<td>Lumbar</td>
<td>Opioid alone</td>
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<td>327</td>
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<td>12.0 (0.6)</td>
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</table>

Abbreviations: CI, confidence interval; VAS, visual analog scale.

*Mean VAS and SEM include both rest and incident pain. Weighted mean differences between epidural analgesia and parenteral opioids (positive numbers favor epidural analgesia) were rounded.
Complications
Not every article reported all possible complications. Sixty-nine articles (56%) reported the incidence of at least 1 major complication and 86 (69%) reported the incidence of at least 1 minor complication. A complication rate of 0% was not assumed if studies failed to report a particular complication. Rates for all complications were relatively low (Table 4).

Motor block was the adverse effect most attributable to epidural analgesia. Lumbar epidural analgesia with opioid alone also had a higher rate of numbness. This was unexpected because epidural opioid alone should not cause numbness; however, this finding probably reflected the results of only 1 study in which epidural morphine was delivered by bolus for analgesia after use of

Table 3. Analgesia by Surgical Site, Epidural Location, and Infusion Categorized by Rest and Incident Pain

<table>
<thead>
<tr>
<th>Surgical Site</th>
<th>Complication</th>
<th>Epidural Location</th>
<th>Epidural Infusion</th>
<th>No. of Studies</th>
<th>No. of Observations</th>
<th>Parenteral Mean VAS (SEM), mm</th>
<th>Epidural Mean VAS (SEM), mm</th>
<th>Weighted Mean Difference (95% CI), mm</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thoracic</td>
<td>Nausea or vomiting</td>
<td>Thoracic</td>
<td>Local anesthetic with or without opioid</td>
<td>10</td>
<td>694 Rest</td>
<td>21.9 (0.6)</td>
<td>11.3 (0.4)</td>
<td>10.7 (9.3-12.0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Opioid alone</td>
<td>6</td>
<td>443 Incident</td>
<td>36.2 (0.8)</td>
<td>24.7 (0.7)</td>
<td>11.5 (9.4-13.6)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Opioid alone</td>
<td>7</td>
<td>162 Rest</td>
<td>12.1 (0.3)</td>
<td>11.5 (0.4)</td>
<td>0.6 (-3 to 1.5)</td>
<td>.12</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Opioid alone</td>
<td>5</td>
<td>122 Incident</td>
<td>41.3 (0.5)</td>
<td>35.5 (1.0)</td>
<td>5.9 (3.6-8.2)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>Pruritus</td>
<td>Thoracic</td>
<td>Local anesthetic with or without opioid</td>
<td>6</td>
<td>374 Rest</td>
<td>19.4 (0.9)</td>
<td>13.7 (0.7)</td>
<td>5.7 (3.5-8.0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Opioid alone</td>
<td>9</td>
<td>208 Incident</td>
<td>19.4 (0.9)</td>
<td>13.7 (0.7)</td>
<td>5.7 (3.5-8.0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>Infection</td>
<td>Thoracic</td>
<td>Local anesthetic with or without opioid</td>
<td>12</td>
<td>1141 Rest</td>
<td>18.9 (0.3)</td>
<td>9.0 (0.2)</td>
<td>9.9 (3.9-10.4)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Opioid alone</td>
<td>4</td>
<td>144 Rest</td>
<td>26.5 (1.0)</td>
<td>20.0 (0.9)</td>
<td>6.5 (3.9-9.0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>Motor block or numbness</td>
<td>Thoracic</td>
<td>Local anesthetic with or without opioid</td>
<td>4</td>
<td>140 Incident</td>
<td>50.0 (1.5)</td>
<td>43.1 (0.9)</td>
<td>6.9 (3.4-10.6)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Opioid alone</td>
<td>4</td>
<td>140 Incident</td>
<td>50.0 (1.5)</td>
<td>43.1 (0.9)</td>
<td>6.9 (3.4-10.6)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Table 4. Complication Rates

<table>
<thead>
<tr>
<th>Complication</th>
<th>Epidural Site</th>
<th>Epidural Infusion</th>
<th>No. of Studies</th>
<th>Patients at Risk</th>
<th>Incidence Rates</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea or vomiting</td>
<td>Thoracic</td>
<td>Local anesthetic with or without opioid</td>
<td>29</td>
<td>717</td>
<td>26/376</td>
<td>.61</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Opioid alone</td>
<td>12</td>
<td>191</td>
<td>5/25</td>
<td>.02</td>
</tr>
<tr>
<td></td>
<td>Lumbar</td>
<td>Local anesthetic with or without opioid</td>
<td>16</td>
<td>321</td>
<td>42/376</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Opioid alone</td>
<td>37</td>
<td>704</td>
<td>60/38</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Pruritus</td>
<td>Thoracic</td>
<td>Local anesthetic with or without opioid</td>
<td>29</td>
<td>717</td>
<td>2/376</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Opioid alone</td>
<td>12</td>
<td>191</td>
<td>7/0</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>Lumbar</td>
<td>Local anesthetic with or without opioid</td>
<td>16</td>
<td>321</td>
<td>2/376</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Opioid alone</td>
<td>37</td>
<td>704</td>
<td>6/38</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Motor block or numbness</td>
<td>Thoracic</td>
<td>Local anesthetic with or without opioid</td>
<td>29</td>
<td>717</td>
<td>2/376</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Opioid alone</td>
<td>12</td>
<td>191</td>
<td>0/0</td>
<td>&gt;.99</td>
</tr>
<tr>
<td></td>
<td>Lumbar</td>
<td>Local anesthetic with or without opioid</td>
<td>16</td>
<td>321</td>
<td>1/376</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Opioid alone</td>
<td>37</td>
<td>704</td>
<td>0/7</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Hypotension</td>
<td>Thoracic</td>
<td>Local anesthetic with or without opioid</td>
<td>29</td>
<td>702</td>
<td>14/376</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Opioid alone</td>
<td>12</td>
<td>190</td>
<td>0/0</td>
<td>&gt;.99</td>
</tr>
<tr>
<td></td>
<td>Lumbar</td>
<td>Local anesthetic with or without opioid</td>
<td>16</td>
<td>350</td>
<td>8/376</td>
<td>.03</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Opioid alone</td>
<td>37</td>
<td>698</td>
<td>1/3</td>
<td>.04</td>
</tr>
</tbody>
</table>
epidural local anesthetic anesthesia for cesarean delivery. Nausea or vomiting rates were significantly lower with local anesthetic–based LEA compared with parenteral opioids but not for TEA with local anesthetic with or without opioid or LEA with opioid alone. For pruritus, LEA with opioid alone had a 6-fold increased incidence from parenteral opioid. Thoracic epidural analgesia with local anesthetic with or without opioid had increased rates of hypotension compared with parenteral opioid but the overall incidence of hypotension was low. Insufficient data were available to determine the effect of postoperative epidural analgesia on return of function, major complications, and some minor complications (confusion-delirium, sedation, constipation, urinary retention, headache, and backache).

COMMENT

Compared with parenteral opioids, epidural analgesia overall provided significantly better postoperative analgesia. Epidural analgesia also provided significantly better postoperative analgesia at all intervals up to 4 days after surgery. When analyzed according to type of analgesic agent (local anesthetic with or without opioid vs opioid alone), location of catheter insertion and site of surgical incision (thoracic vs lumbar), and type of pain assessment (rest vs incident/dynamic pain), epidural analgesia in every combination, with the exception of TEA with opioid for thoracic surgery, provided better postoperative analgesia compared with parenteral opioids. Greater improvements were found in analgesia when local anesthetic was included in the epidural regimen, implying that epidural opioid alone may not be better than parenteral opioid and general decreases in rates of complications with thoracic, instead of lumbar, epidural placement.

There are several reasons that epidural analgesia may confer better postoperative analgesia compared with parenteral opioids. Epidural local anesthetics may attenuate or block painful input into the central nervous system and addition of an epidural opioid may result in a synergistic analgesic effect. Individual RCTs also have demonstrated that epidural infusions of local anesthetic-opioid combinations provide better analgesia compared with intravenous PCA with opioids, though the incidence of clinically relevant hypotension may be quite different (higher) in actual clinical practice. In addition, our incidence of lower extremity motor block (1%-2%) was comparable with large observational data of postoperative epidural analgesia using a local anesthetic-based solution (approximately 2%-3%). Physicians caring for postoperative patients should be aware that lower extremity motor block may be an early indicator of epidural hematoma development in patients receiving both epidural analgesia and anticoagulants.

Limitations

There are several limitations to this study. Despite the relatively large number of patients studied, a reduction in mean VAS ranging from 2.2 mm to 19.9 mm may be clinically meaningful. Although we were unable to compare other important pain outcome measures, such as percentage of maximum total pain relief, sum of the pain intensity difference, or percentage pain intensity difference because of the limitations of the available data, we did note an approximate 30% to 33% relative to the variability in the definition of these events with RCTs possibly having a lower incidence because of the presence of more stringent event definitions. The incidence of nausea or vomiting (5%-60%) and pruritus (7%-38%) for patients receiving epidural opioid regimens in our trials were lower than that reported in other studies. The cumulative incidence of nausea and vomiting in patients receiving continuous infusions of opioids may be as high as 45% to 80%. Pruritus is one of the most common adverse effects from epidural administration of opioids with an incidence of approximately 60% compared with an incidence of approximately 15% for those patients receiving systemic opioids.

The incidence of hypotension with a local anesthetic-based epidural regimen in our study (8%-14%) is higher than that reported in large-scale observational studies of postoperative epidural analgesia (0.7%-3.0%), although the incidence of clinically relevant hypotension may be quite different (higher) in actual clinical practice. In addition, our incidence of lower extremity motor block (1%-2%) was comparable with large observational data of postoperative epidural analgesia using a local anesthetic-based solution (approximately 2%-3%). Physicians caring for postoperative patients should be aware that lower extremity motor block may be an early indicator of epidural hematoma development in patients receiving both epidural analgesia and anticoagulants.

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(Reprinted) JAMA, November 12, 2003—Vol 290, No. 18 2461
duction in pain ratings (a value suggested to be a clinically relevant reduction in pain scores) for epidural analgesia vs systemic opioids.

Although the data were weighted by trial size, they were not weighted by the quality of the RCTs used nor were they assessed in a blinded fashion. Some authors suggest that assessing the quality of RCTs used in a meta-analysis or reports of RCTs in a blinded fashion will influence the estimate of intervention efficacy reported in a meta-analysis. However, others indicate that individual quality measures are not reliably associated with the strength of treatment effect in a meta-analysis. We believe that the quality of the included RCT is generally similar, as all the trials were randomized and controlled but not consistently double-blinded, a widely recognized limitation of RCTs examining perioperative epidural analgesia to systemic opioids.

We limited our meta-analysis to English-language articles. Although the effect of excluding non-English trials on the results of a meta-analysis is unclear, in some cases excluding trials published in other languages may have little effect on summary treatment effects and may actually result in a more conservative estimate of treatment effect. For our meta-analysis, only 9 non-English articles would have qualified for inclusion, and the introduction of these articles (7 of which showed that epidural analgesia produced better analgesia) would not have changed our results. Assessing the generalizability of the results is difficult because the protocolization of postoperative analgesic care in randomized trials tends to skew delivery of typical patient care and our results may not be applicable to the general clinical population. Specifically, epidural analgesia can fail because of technical reasons in as often as 6% to 25% of cases, with many centers reporting failure rates between 10% to 20%.

Conclusion

In conclusion, epidural analgesia (other than TEA with opioids for thoracic surgery) provided a statistically and clinically significant improvement in postoperative pain control compared with parenteral opioids, regardless of analgesic regimen (local anesthetic with or without opioid or opioid alone), site of epidural catheter placement in relation to the surgical incision, or measured pain outcomes (rest or incident pain). With approximately 40 million inpatient surgical procedures performed in the United States annually and the recent emphasis on pain control with the introduction of JCAHO guidelines for the assessment and management of pain, physicians should be aware of the analgesic benefits and potential risks of epidural analgesia when discussing options for postoperative pain management with their patients.


Study supervision: Liu, Wu.

Acknowledgment: We thank John McCready, MS, in the Department of Biostatistics at Johns Hopkins Bloomberg School of Public Health and Lee Fleisher, MD, Director of the Perioperative Clinical Research Unit in the Department of Anesthesiology and Critical Care Medicine at Johns Hopkins University for their assistance.

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of reports of randomised trials affect estimates of in-
tervention efficacy reported in meta-analyses? Lan-
quality of reports of randomized clinical trials: is blind-
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effect in meta-analyses of randomized controlled trials.
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impact of language bias in meta-analyses of con-
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ceiving postoperative patient-controlled epidural an-

Be it grand or slender, burrowing, blasting, or refusing
to sanctify; whether it laughs out loud or is a cry
without an alphabet, the choice word or the chosen
silence, un molested language surges toward knowl-
edge, not its destruction.
—Toni Morrison (1931- )