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Epidural analgesia versus intravenous patient-controlled analgesia following minimally invasive pectus excavatum repair: a systematic review and meta-analysis

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ABSTRACT

Background/Purpose: The minimally invasive pectus excavatum repair (MIPER) is a painful procedure. The ideal approach to postoperative analgesia is debated. We performed a systematic review and meta-analysis to assess the efficacy and safety of epidural analgesia compared to intravenous Patient Controlled Analgesia (PCA) following MIPER.

Methods: We searched MEDLINE (1946–2012) and the Cochrane Library (inception–2012) for randomized controlled trials (RCT) and cohort studies comparing epidural analgesia to PCA for postoperative pain management in children following MIPER. We calculated weighted mean differences (WMD) for numeric pain scores and summarized secondary outcomes qualitatively.

Results: Of 699 studies, 3 RCTs and 3 retrospective cohorts met inclusion criteria. Compared to PCA, mean pain scores were modestly lower with epidural immediately (WMD −1.04, 95% CI −2.11 to 0.03, $p = 0.06$), 12 hours (WMD −1.12; 95% CI −1.61 to −0.62, $p < 0.001$), 24 hours (WMD −0.51, 95%CI −1.05 to 0.02, $p = 0.06$), and 48 hours (WMD −0.85, 95% CI −1.62 to −0.07, $p = 0.03$) after surgery. We found no statistically significant differences between secondary outcomes.

Conclusions: Epidural analgesia may provide superior pain control but was comparable with PCA for secondary outcomes. Better designed studies are needed. Currently the analgesic technique should be based on patient preference and institutional resources.

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Pectus excavatum is the most common congenital chest wall deformity, occurring in approximately 1 out of every 1000 live births [1]. The surgical repair of this deformity has seen several adaptations during its evolution: most recently the minimally invasive pectus excavatum repair (MIPER), introduced in 1998 [2]. Reported benefits of MIPER include smaller incisions, decreased blood loss, no need for cartilage resection, and reduced operating times [2]. Despite its classification as "minimally invasive," the immediate reshaping of the chest wall during the procedure results in significant post-operative pain [3]. Pain management after MIPER is a challenge and is the primary factor determining the length of hospital stay [4,5].

Epidural analgesia and Patient Controlled Analgesia (PCA) are both widely employed techniques for postoperative pain management [6]. PCA has the advantage of allowing patients to titrate the level of medication, balancing analgesia against sedation [7]. This less invasive technique has been shown to achieve safe and effective analgesia in children [7]. However, the negative side effects of opioid medications, such as respiratory depression, urinary retention, pruritus, nausea, and vomiting can limit its effectiveness in some children [8]. Epidural analgesia is also established as a safe and effective method for postoperative pain management in children [9]. Studies in adult patients suggest epidural analgesia may provide more complete pain relief while avoiding some of the side effects of intravenous opioid infusion [8]. Epidural analgesia is an invasive procedure and is not free of risks such as infections, nerve damage, drug errors, and cardiac or respiratory arrest [10]. Application of this technique also requires experienced and dedicated pediatric anesthesia staff to place the epidural catheter and continue its management post-operatively [3]. Given that both epidural and patient-controlled analgesia have risks and benefits, there is no consensus in the current literature as to which method offers superior pain management following pectus excavatum repair [4,5,11,12].

We systematically reviewed the current evidence comparing epidural analgesia to PCA following minimally invasive pectus excavatum repair. Using these results, we hope to better inform surgeons, anesthesiologists, patients, and their families as they consider options for pain management following MIPER.

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1. Methods

1.1. Review protocol

Prior to conducting our systematic review we created a protocol that outlined our planned approach to the identification and selection of studies. We used the methodology of the Cochrane Handbook for Systematic Reviews of Interventions to identify appropriate studies.

Our pre-specified inclusion criteria were: 1) subjects must be children, adolescents, or young adults (mean age <18 years) undergoing MIPER, 2) one study arm receives epidural analgesia for postoperative pain control, 3) a second study arm receives intravenous PCA analgesia, 4) the study design is either a randomized controlled trial (RCT) or a cohort study, and 5) authors must report at least one of our pre-specified outcomes of interest.

1.2. Outcome measures

Our primary outcome measure was postoperative numeric pain scores. Pain scores were reported on a numerical scale, 0–10 in all included studies.

In order to investigate the efficacy and safety of the two analgesic methods, we divided our secondary outcomes into benefits and harms. Benefits included 1) overall costs, including costs related to operating room time, length of hospital stay, and adverse events, 2) length of hospital stay, 3) duration of treatment and 4) use of rescue analgesics. Harms included 1) epidural related complications, 2) epidural failure or inability to place an epidural and 3) opioid-related side effects.

1.3. Search methods

1.3.1. Databases, search terms, limits, and special strategies

We searched two electronic databases MEDLINE (1946 through September 2012) and the Cochrane Library (all databases, Inception through October 2012). We used exploded Medical Subject Headings (MeSH) and keywords to generate sets for the following themes: Pediatrics, Post-Operative Pain Control, and Minimally Invasive Pectus Excavatum Repair and then the Boolean operator "AND" to find their intersection. We consulted an experienced reference librarian and used no limits or language restrictions. We conducted a review of the references from each included study and searched for unpublished studies using clinicaltrials.gov and Controlled-Trials.com. Our search strategy is included as Appendix 1.

1.4. Study selection

Two authors independently screened all titles and abstracts from the initial search, only excluding those that were clearly ineligible. The same two reviewers performed a full text review of the remaining studies to assess for final eligibility. Non-English language studies were translated and articles by the same author were specifically reviewed for overlapping study populations to prevent duplicate reporting [13–18]. At each step of eligibility screening, we resolved disagreements by discussion, involving a third author if necessary to reach consensus.

1.5. Assessment of methodological quality

The methodological quality of included studies was assessed using both the Cochrane risk of bias tool and the Newcastle-Ottawa Quality Assessment Scale for Cohort Studies as our review included both randomized trials and cohort studies [19,20]. For the Cochrane risk of bias tool we evaluated studies based on randomization, blinding of outcome assessment, completeness of outcome assessment, and selective reporting. We used the Newcastle-Ottawa scale to assess studies in 8 categories, which considered assessment of exposure, outcome, selection, comparability, and follow-up. The impact of methodological quality on summary estimates was evaluated using sensitivity analysis.

1.6. Analysis

1.6.1. Measure of treatment effect

We summarized the numeric pain score results of the included studies using weighted mean differences (WMD). The WMD is a statistic that measures the absolute difference in mean value between two groups in a clinical trial and uses the standard deviation and sample size to calculate the weight given to each study [19]. When pain scores were not presented in table format, we extrapolated pain scores from graphs [4,5,11,12,17]. For one study that reported medians, we estimated the standard deviation using inter-quartile ranges, employing formulas provided in the Cochrane Handbook [12,19]. When standard deviations were not reported, we used an average of the standard deviations from the studies that had reported standard deviation [4,5,11].

Secondary outcomes were inconsistently measured and reported across studies; therefore, we analyzed these results qualitatively. For each reported secondary outcome, we compared the point estimate for the epidural arm to the point estimate for the PCA arm in each study to determine, which arm, if any, was favored. We then examined across all studies reporting the outcome to determine, qualitatively, if epidural, PCA, or neither was favored. When a measure of statistical significance was provided, we incorporated this in our analysis. We assessed the epidural failure rate by evaluating the overall percent of reported epidural failures as well as individual author's qualitative description of this outcome.

1.6.2. Data synthesis

For our primary outcome, we used RevMan 5 software (Cochrane Information Management System) to pool individual study results, weighted by the inverse variance method, and calculate summary statistics and 95% confidence intervals. Since significant heterogeneity was present, we performed this analysis using a random-effects model, which assumes that the individual studies are estimating effects that are not identical, but follow some distribution [19]. As this model takes heterogeneity between studies into account, it is considered to be a more conservative estimate.

1.6.3. Assessment of heterogeneity

We assessed heterogeneity across studies by using I^2 statistics, where a value greater than or equal to 50% indicates a significant level of heterogeneity, and the calculated test for heterogeneity p value, where significant heterogeneity is indicated by a p value less than 0.10. If significant heterogeneity was present, we evaluated the individual studies in order to identify outliers. When outliers were identified, we evaluated study characteristics for sources of heterogeneity. We performed sensitivity analysis when heterogeneity was present by sequentially excluding individual outliers. If we were unable to achieve homogeneity after study exclusion, we still reported our summary estimate and noted heterogeneity. For qualitative analyses, we assessed for heterogeneity by visually inspecting our summary tables for possible outliers.

1.6.4. Assessment of reporting bias

Using RevMan 5 software, we evaluated for publication bias by creating a funnel plot for our primary outcome measure. The funnel plot displays the effect size for pain scores at different time points versus sample size for each study. Publication bias is considered unlikely if the funnel plot appears symmetric on visual inspection [19].