Comparison of regional vs systemic analgesia for post-thoracotomy care in infants

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Keywords
anesthetic techniques; regional; thoracic; analgesia; epidural; infant; newborn; postoperative care; thoracotomy

Summary

Background: In infants, post-thoracotomy analgesia traditionally consists of systemic opiates, while regional techniques have gained more favor in recent years. We compare the two techniques for thoracotomy in infants.

Methods: All consecutive patients below 6 months of age who underwent thoracotomy for congenital pulmonary malformations in the study period were retrospectively divided according to the chosen postoperative analgesia: Group S systemic opiates, Group R continuous regional (epidural or extra-pleural paravertebral) block. We studied the following outcomes: need for NICU and mechanical ventilation, pain score, requirement for additional analgesics, heart rate 1 h postsurgery, time to pass first stool and to full feed, complications, and duration of hospitalization.

Results: Forty consecutive patients were included, 19 in Group S and 21 in Group R. Median age at surgery was 89 days (40–110) and 90 days (46–117), respectively. Five of 19 patients in Group S vs none in Group R required postoperative intensive care (P = 0.017). Patients in Group R had significantly lower postoperative heart rate (145 [138–150] vs 160 [152–169] b/min⁻¹, P = 0.007), earlier passage of first stools (24 h [12–24] vs 36 h [24–48] P = 0.004), and earlier time to full feed (36 h [24–48] vs 84 h [60–120] P = 0.0001) than those in Group S. The only observed complication was one catheter dislocation.

Conclusion: In infants undergoing thoracotomy, loco-regional analgesia is effective and associated with a reduced intensity of postoperative care and earlier full feeding than systemic analgesia; it should therefore be considered a better option.

Background

Thoracotomy may lead to severe postoperative complications such as atelectasis, pneumonia, pulmonary embolism, and emergency intensive care admission, all of which may be due, at least in part, to poor analgesia and its correlated thoracic immobility (1,2). In adults and older children, the severe complications of post-thoracotomy pain have brought about an aggressive search to improve treatment modalities, including the use of thoracic epidural analgesia and thoracic paravertebral block (PVB), which have shown great benefits over systemic anesthesia, with a comparable or improved safety profile (1–3).

As a consequence, these regional techniques have now become the recommended standard anesthesia–analgesia in adults (4,5). These regional techniques have in time trickled down to the pediatric sphere (6–8). With regard to neonates and small infants, however, the adoption of regional analgesia for thoracic surgery has been slowed by perceived and real difficulties with technical equipment and fears of complications, as expressed recently by Bösenberg Jöhr and Wolf (9). In addition, the relatively small number of
infants requiring this approach may lead to insufficient experience by providers who are not in large pediatric referral centers, thereby increasing the potential for complications (9,10). In newborns and infants, central neuraxial anesthesia is now commonly used at the lumbar level for low-abdominal or inguinal surgical procedures (11), but less so for thoracic-level procedures; in this age group, a lumbar- or caudal-approach epidural is often chosen for abdominal or thoracic cases, threading the catheter cephalad to the appropriate level.

Regional thoracic-level techniques are now gaining wider acceptance in infants. If a principal focus of anesthesia is preserving physiologic stability and reducing postoperative pain and stress, this would seem particularly important in small infants who, due to their weak musculature and immature respiratory system, are particularly susceptible to the impairment of pulmonary function caused by thoracotomy and its associated pain. Clinical studies suggest that continuous infusion of local anesthetic in both the paravertebral space (8,12) and the epidural space (13–15) is effective in the management of post-thoracotomy analgesia and helps attenuate perioperative stress in small infants and neonates.

The aim of our study was to evaluate the safety and effectiveness of regional block, in the form of thoracic-level epidural or extrapleural paravertebral analgesia, as compared to systemic analgesia for postoperative care in infants undergoing thoracotomy for congenital pulmonary malformations (CPM).

Methods

All patients under 6 months of age who consecutively underwent thoracotomy for CPM between February 2009 and June 2012 were included in this retrospective study. Patients were retrospectively divided into two groups according to the type of analgesia chosen at the time of surgery for postoperative pain control: Group S was treated with systemic opiates, and Group R with regional analgesia. The latter was obtained via continuous infusion of ropivacaine, either with a PVB, via subpleural catheter placed by the surgeon at the end of the surgical procedure, or as epidural block, via a catheter placed by the anesthesiologist at the start of the surgical procedure. The anesthesia modality was chosen by the team at the time of surgery, as during the study period our center transitioned from general systemic to thoracic loco-regional as the ‘usual’ modality of analgesia for this type of surgery. Only two anesthesiologists with specific neonatal expertise managed these patients intraoperatively.

Our main outcome measure was requirement for postoperative neonatal intensive care unit (NICU) admission and/or mechanical ventilation. This option was chosen by the team at the end of the surgical procedure depending on the respiratory and cardiovascular status of the baby, apneas, and continued need for respiratory support. In our center, the alternative to NICU for these patients is an intermediate-care neonatal ward with continuous monitoring of cardiorespiratory parameters. We also compared secondary outcomes between the two groups: heart rate 1 h after surgery, postoperative pain score, requirement for additional analgesia, time to pass first stools and to full feeding, prevalence of complications, and duration of postsurgical hospital stay. Postoperative monitoring included pulse oximetry, electrocardiography, arterial blood pressure, temperature, and urine output.

Postoperative pain was measured by trained nurses every 4 h for 72 h using the CRIES scale (16) (Crying, Requires increased O2 administration, Increased vital signs, Expression, Sleepiness). When the CRIES score was above 5, paracetamol (10 mg·kg⁻¹ i.v., max tid) was administered in both the groups to the baseline therapy of continuous i.v. morphine or continuous regional infusion of ropivacaine, respectively. In addition to the pain score itself, the requirements for additional analgesia were also documented for each patient. Mann–Whitney U-test or chi-square test was used as appropriate. Results are expressed as medians (IQR range) or prevalence; two-tailed P < 0.05 was considered significant.

Techniques

In all patients, initial induction was achieved through inhalation of sevoflurane in an air–oxygen mixture and a single intravenous morphine bolus (0.01 mg·kg⁻¹), and the baby was intubated. For induction, morphine was preferred to fentanyl to reduce the risk of chest wall rigidity and of hemodynamic instability associated with this medication.

Thoracic epidural anesthesia and analgesia (TEA)

The baby was anesthetized (sedated, intubated, not paralyzed) and placed on left side with hips and knees bent at 90°. Under sterile conditions, an epidural catheter (Polymedic 20-gauge Tuohy needle) was inserted parallel to the plane of the bed in the midline at the T7/T8 intervertebral space, at an angle of 60° with the bevel facing cranially. Once the epidural space was identified, a single bolus of 2 mg·kg⁻¹ of ropivacaine (Naropin®, AstraZeneca, Basiglio (MI, Italy) 0.4%) was injected slowly (90 s), followed by a continuous infusion of ropivacaine 0.125%/h at 0.2 mg·kg⁻¹·h⁻¹ for postoperative pain control. The concentration of 0.4%
for the initial bolus was chosen to reduce the injected volume, thereby reducing the risk of cephalad diffusion. The catheter was removed 72 h postoperatively.

Interpleural paravertebral block
The baby was anesthetized, sedated, intubated for the procedure. Toward the end of the surgical procedure, the surgeon guided the tip of an externally inserted catheter (the same type as that used for the epidural block) under direct vision through the open thorax into a localized extrapleural paravertebral pocket. As for the epidural block, an initial bolus of ropivacaine was followed by continuous infusion through the catheter (at the same concentration and infusion rates mentioned above) until its removal 72 h postoperatively.

Systemic analgesia
Intraoperative analgesia consisted of morphine infusion 0.1 mg kg\(^{-1}\) h\(^{-1}\) and sevoflurane inhalation at 2.5%.
Postoperative pain was managed with an intravenous morphine drip (initially 0.01 mg kg\(^{-1}\) h\(^{-1}\)) until 24 h, followed by progressive weaning and titration according to pain score, and discontinuation by 72 h postoperatively.

Results
In the study period, 40 consecutive patients underwent surgery for CPM, 19 in Group S, and 21 in Group R. In the regional analgesia group, 11 had a thoracic epidural, and 10 a PVB. As shown in Table 1, gestational age at birth, median age and weight at surgery, and gender distribution were similar between the two groups. All patients had an antenatal diagnosis of CPM confirmed after birth. In Group R, 17 patients had congenital cystic adenomatoid malformation of the lung (CCAML), three had a pulmonary sequestration (PS), and one congenital lobar emphysema. In Group S, nine patients had CCAML, five had PS, while five had a mixed lesion with CCAML areas within a PS. All patients underwent thoracotomy. A lobectomy was performed in all patients except for three in Group S who underwent PS removal.

The main findings are shown in Table 2. None of the patients in Group R required postoperative mechanical ventilation, while 5 of 19 babies (26%) in Group S required an average of 72 h (range 12–432) of mechanical ventilation (\(P = 0.018\)). In the postoperative period, Group S patients showed statistically significant higher heart rate, delayed passage of first stools, and delayed full enteral feeding as compared to Group R. No difference was found between the two groups in highest pain score or in requirements for additional analgesics, nor in duration of chest drain. The postoperative length of hospital stay was shorter in Group R, although this difference did not reach statistical significance. In Group R, no second attempt was necessary for catheter insertion, and none required early removal for leakage, migration, or malposition. One epidural catheter dislocated before the intended removal time. None of the patients had intraoperative complications, hemodynamic instability, nor postoperative complications or side effects related to catheter placement.

Discussion
Our study adds to the growing number of publications (12,14,17,18) which demonstrate that continuous catheter regional analgesia in small infants can achieve pain control which is at least equivalent to that of systemic opiates, all the while reducing potential side effects and the intensity of postoperative care. Extrapleural paravertebral thoracic analgesia in infants was first described by Karmakar’s group (12,18) in 1996 and Vane in 1997 (19). The effectiveness of epidural

| Table 1 | General characteristics of patients undergoing systemic (Group S) or loco-regional (Group R) analgesia. Results are medians (interquartile ranges) |
|---|---|---|
| Group S (19 patients) | Group R (21 patients) | \(P\) value |
| Sex (M/F) | 11/8 | 11/10 | 0.7605 |
| Gestational age (weeks) | 39.0 (38.0–40.0) | 38.0 (37.0–39.5) | 0.3119 |
| Age at surgery (days) | 89 (40–110) | 90 (46–117) | 0.7863 |
| Weight at surgery (kg) | 5.8 (5.5–6.3) | 6.1 (4.7–6.8) | 0.4897 |

| Table 2 | Main outcomes in patients undergoing systemic (Group S) or loco-regional (Group R) analgesia. Results are medians (interquartile ranges) or prevalence |
|---|---|---|
| Group S (19 patients) | Group R (21 patients) | \(P\) value |
| Post-op. intensive care (%) | 5/19 (26.3) | 0/21 (0) | 0.0177 |
| Heart rate 1 h post-op. (b min\(^{-1}\)) | 160 (152–169) | 145 (138–150) | 0.0075 |
| Post-op. first stool (h) | 36 (24–48) | 24 (12–24) | 0.0039 |
| Post-op. full feed (h) | 84 (60–120) | 36 (24–48) | <0.0001 |
| Additional post-op. analgesia (doses) | 1 (0–2) | 1 (0–3) | 0.8776 |
| Post-op. drain duration (h) | 120 (96–192) | 113 (84–120) | 0.1476 |
| Post-op. hospital stay (days) | 7 (6–11) | 6 (5–8) | 0.0896 |
related stress response in neonates and small infants has been demonstrated (14,15,17); however, only a small proportion of these described cases was thoracic-level epidurals, and most of them were low thoracic. Since those early studies, little has been published regarding regional analgesia for post-thoracotomy care in neonates and infants. Our study is one of few in the literature to describe a uniform group of small infants undergoing a single type of surgery (thoracotomy for pulmonary malformation), and with a high-level (T7/T8) thoracic epidural or PVB.

Our most significant result is the decreased need for postoperative intensive care and mechanical ventilation in the regional analgesia group as compared to the systemic opioid group. This improvement in postoperative care, which is coherent with the literature regarding adults and children (3,5,9), may be due to lower surgery-related stress response – in the TEA subgroup – or less pain leading to more comfortable breathing. Furthermore, both failure to wean to extubation and opioid-induced apnea episodes are also well described in babies treated with systemic opioid anesthesia. Our study supports the hypothesis that regional catheter analgesia with local anesthetics allows good pain control while bypassing these significant respiratory opioid-induced complications. Earlier extubation and decreased NICU stays are not only of benefit in and of themselves, but may, in turn, contribute to diminished costs, risks of nosocomial infections, total duration of hospitalization, and patient and family stress.

Another interesting result is the difference in gastrointestinal consequences of surgery and anesthesia. The infants receiving catheter analgesia were able to be fed sooner and had improved intestinal motility. These results are consistent with previous reports (3,9) and support the principle that the use of regional analgesia avoids the inhibitory effects of opioids on intestinal motility, contributing to earlier re-feeding. In infants as in older children and adults, regional analgesia seems to bring about an ideal analgesia where the pain is well treated with no negative effects on respiratory drive or intestinal motility.

Our results show similar pain scores and requirements for additional analgesia between the two groups, demonstrating that the pain control achieved through regional analgesia is at least equivalent to that obtained with the more commonly used systemic opiates. The adequacy of analgesic effect of epidural or PVBs in infants has been previously shown (12,15,17,18). Pain is a key component in the alteration of lung function after thoracic surgery (20), and its inadequate management and consequently augmented stress response may lead to prolonged postsurgical recovery, as well as elaboration of new pain pathways which alter pain responses later in life. Some studies (5,7,12,18) actually show excellent pain control with regional anesthesia alone, or improved analgesia with regional vs systemic therapy; our groups did not show such a difference. This might be explained by the fact that although the pain scale we used (CRIES) is a validated (16) clinical method to measure pain in infants, there is indeed a subjective component, due to the patients’ inherent immature communication skills and the overlay of interpretation by the nurse, which can be influenced by several factors (presence of the parents by the bedside, personal attitudes toward pain, time of day, anxiety, etc.). The difference between the two groups in heart rate measurement, which may be interpreted as a proxy for pain, may be an indicator of truly decreased pain in the regional analgesia group vs the systemic group. The difference in heart rate may however also be explained by the deactivation of the sympathetic fibers in the paravertebral or epidural blocks, although resting sympathetic tone is not yet fully developed in this age group. Although based on our findings we cannot say that the analgesia of regional techniques is superior to systemic opioids, we believe the superiority of regional analgesia is underlined here by the reduced need for postoperative intensive care and earlier full feeding and passage of stool.

The final important result of the study is the absence of significant complications related to catheter placement or medication used in the loco-regional analgesia group, except for one catheter dislocation prior to the intended removal time, which did not result in any sequelae. There was no evidence of anesthetic toxicity, accidental intravascular injection of anesthetic, infection, catheter migration, or nerve injury. Given the very low reported risk of complications with these procedures (17,21), our small sample size does not permit any safety conclusions but contributes nonetheless to the literature of encouraging safety profiles for both types of regional analgesia in infants. A recent study (22) also confirmed that when infusion rates of 0.2 mg kg⁻¹ h⁻¹ of ropivacaine are used for epidurals in infants, the serum levels of the anesthetic are kept within an acceptable range and medication-related complications can be avoided. However, further studies are needed to verify the degree of absorption and potential toxicity of ropivacaine in PVBs on small infants, as the vascularity and spatial distribution of the paravertebral space differ from those of the epidural space.

The main limitation of this study is its retrospective nature: The patients were not randomized a priori. The type of anesthesia to administer was chosen by the team intraoperatively, and this may have led to a selection bias in our results. Another limitation is that...
Group R clustered together two types of regional analgesia: epidural and PVBs. These procedures are carried out by different figures in the operating room (the anesthesiologist and the surgeon, respectively) and, although similar in effect, carry different degrees of difficulty and potential risks. A further potential limitation is that the small number of patients and of anesthetists involved in the study may limit reproducibility of the results. However, we believe that our results are indeed reproducible in pediatric hospitals where most anesthesiologists are familiar with thoracic epidural analgesia.

Our study adds to the increasing evidence that high-level thoracic epidural and extrapleural PVBs are safe and effective in very young infants, including in thoracic surgery, improving global postoperative outcomes and avoiding the complications of systemic analgesia, which are significant in this age group. Further research is needed, comparing each modality of post-thoracotomy analgesia in a prospective randomized trial in newborns and infants.

Funding
This research was carried out without funding.

Conflict of interest
Each author declares the absence of any conflict of interest relating to this article.

References