

The Use of Regional Anesthesia in Combination with General Anesthesia for Cardiac Surgery in Children

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Introduction

The use of regional anesthesia in combination with general anesthesia for children undergoing cardiac surgery is the subject of a growing number of publications and presentations. Reported benefits of regional anesthesia in patients having cardiac surgery include attenuation of the neuroendocrine response to surgical stress, improved postoperative pulmonary function, enhanced cardiovascular stability, and improved postoperative analgesia. To the extent that regional anesthesia facilitates early tracheal extubation in cardiac surgical patients, complications and costs associated with postoperative mechanical ventilation may be reduced. These benefits must, however, be weighed against the adverse effects which may accompany the use of regional anesthesia. These include hypotension, postoperative respiratory depression, and epidural hematoma formation. In this article, the benefits and risks of regional anesthesia in infants and children having open heart surgery are reviewed. In addition, specific techniques currently in use are described.

The benefits of regional anesthesia in cardiac surgery

Adverse physiologic responses which occur during and after cardiac surgery include alterations in circulatory (tachycardia, hypertension, vasoconstriction), metabolic (increased catabolism), immunologic (impaired immune response), and hemostatic (platelet activation) systems.^(1,2) Together, these changes are referred to as the “stress response”. The stress response associated with cardiac surgery in neonates may be profound and is associated with increased morbidity and mortality.⁽³⁾ Anand, et. al., measured such responses during and after cardiac surgery in 15 neonates anesthetized with halothane and morphine. They found elevated plasma concentrations of epinephrine, norepinephrine, cortisol, glucagon, and beta endorphin in all patients, accompanied by hyperglycemia and lactic acidemia. The four deaths in the study group occurred in neonates with the greatest stress responses.

Bromage et al., first demonstrated in 1971 that the stress response associated with major abdominal and thoracic surgery could be attenuated with epidural blockade.⁽⁴⁾ Since then, several investigators have shown that the use of regional anesthesia during and after cardiac surgery (i.e. intraoperative anesthesia and post-operative analgesia) may decrease the stress response as well as morbidity and mortality.^(5,6,7,8,9,10,11,12) While these adverse responses can be attenuated with intravenous opioids, regional anesthesia (intrathecal or epidural blockade) with opioids and/or local anesthetics appears to be more effective in inhibiting the stress response associated with surgery. For example, epidural fentanyl is more effective than intravenous fentanyl in reducing the stress response after thoracotomy in adults.⁽¹³⁾ Epidural morphine administration was shown to attenuate the adverse decrease in T3 (liothyronine) concentration in children undergoing open heart surgery compared with general anesthesia alone.⁽¹⁰⁾ Epidural anesthesia with bupivacaine suppresses the increase in serum catecholamines, glucose, and ACTH more effectively than intravenous fentanyl in infants.⁽¹⁴⁾ Epidural local anesthetics may be more efficacious than opioids in attenuating the stress response.⁽¹⁵⁾ In a study of fetal lambs, total spinal anesthesia completely blocked the stress response to surgical manipulation and cardiopulmonary bypass.⁽¹⁶⁾

Additional benefits that may be attributed to regional anesthesia include improved pulmonary function, greater circulatory stability, and reduced pain scores. Several randomized, controlled studies in adults have shown that patients receiving epidural analgesia have better pulmonary function after thoracic surgery than those treated with intravenous opioids. Thoracic epidural opioids are associated with improved pulmonary function following chest surgery compared with IV opioids.⁽¹⁷⁾ In a study comparing thoracic epidural bupivacaine to IV morphine for post-operative analgesia, the

patients receiving epidural infusions had significantly greater FEV₁ and FVC, and were more cooperative with deep breathing maneuvers than those in the IV morphine group.⁽¹⁸⁾ Thoracic epidural anesthesia may also improve respiratory performance postoperatively by effecting an improvement in diaphragmatic function.⁽¹⁹⁾

Several studies in infants and children demonstrate reduced opioid requirements and improved analgesia following cardiac surgery with neuraxial anesthesia. Jones et al., reported the use of intrathecal morphine for postoperative analgesia in 56 children undergoing cardiac surgery.⁽²⁰⁾ Following induction of anesthesia, patients received intrathecal morphine 0.02 or 0.03 mg/kg. Tracheal extubation was performed in all patients after admission to the ICU postoperatively. The duration of analgesia in both groups was similar, with two thirds of patients requiring no supplemental analgesia for more than 18 hours.

In a retrospective review of pain control in 91 children undergoing cardiac surgery, Shayevitz et al., compared lumbar epidural morphine infusions to intravenous opioid analgesia.⁽²¹⁾ In the epidural analgesia group, lumbar epidural catheters were placed following induction of anesthesia. Preservative-free morphine sulfate was administered in a bolus dose of 0.05 mg/kg followed by a continuous infusion of 0.03–0.04 mg/kg/hr during and after surgery. Children in the intravenous analgesia group received an initial IV dose of fentanyl 0.05 mg/kg followed by a continuous infusion of 0.018 mg/kg/hr during surgery. The fentanyl infusion was reduced to 0.006 mg/kg/hr postoperatively. Patients in the epidural analgesia group had significantly lower pain scores and received significantly less supplemental analgesia postoperatively than patients in the intravenous analgesia group.

In a prospective, randomized, controlled study Rosen and Rosen evaluated the efficacy of caudal epidural morphine compared with intravenous morphine in 32 children following open cardiac surgery.⁽²²⁾ Patients in the study group received a caudal injection of preservative-free morphine sulfate (0.075 mg/kg) in the OR following surgery but prior to awakening and tracheal extubation. Patients in the control group received intravenous morphine alone for postoperative analgesia. Supplemental doses of intravenous morphine were given to children in both groups as needed, prior to which pain scores were recorded. Children having received caudal morphine required significantly less intravenous morphine and had significantly lower pain scores postoperatively than patients in the control group. The mean duration of complete analgesia in children receiving caudal morphine was 6 hours (range 2–12 hours), but decreased analgesic requirements were noted for the entire 24 hour study period.

Beside having improved lung function and pain control, patients receiving epidural anesthesia have fewer opioid related side effects than patients treated with intravenous opioids. Patients receiving epidural anesthesia have more rapid return of bowel function following surgery compared with those receiving intravenous analgesics. In a recent review of sixteen studies comparing epidural and systemic analgesia with regard to postoperative recovery of gastrointestinal function, all eight studies with epidural catheter placement above T12 showed more rapid recovery of bowel function when epidural analgesia was used.⁽²³⁾ The use of postoperative thoracic epidural analgesia with bupivacaine and morphine is associated with earlier return of gastrointestinal function and decreased hospital costs due to shortened hospital stay compared with IV morphine patient controlled analgesia.⁽²⁴⁾ A study comparing epidural versus intravenous fentanyl analgesia following thoracotomy also reported a lower incidence of nausea, shorter duration of ileus, and earlier hospital discharge in the epidural analgesia group.⁽¹⁷⁾

Adverse Effects of Regional Anesthesia for Cardiac Surgery

The most serious complications that may be associated with regional anesthesia for cardiac surgery are hypotension, respiratory depression, and epidural hematoma formation.

Systemic arterial hypotension is an undesired effect of intrathecal and epidural local anesthetic blockade. In adults with coronary artery stenosis and myocardial ischemia, local anesthetic-induced blockade of cardiac sympathetic nerve activation alleviates angina and improves coronary blood flow and ventricular function.^(15,25,26,27) However, local anesthetic blockade to upper thoracic dermatomes produces hypotension accompanied by a decrease in coronary artery perfusion.^(28,29) In infants and young children, local anesthetic blockade to T3–T5 does not produce significant changes in blood pressure nor heart rate.⁽³⁰⁾ This may be attributable to decreased sympathetic innervation of the lower extremities and/

or immaturity of the sympathetic nervous system in young children. In a recent study of high spinal blockade in children undergoing open heart surgery, hemodynamic stability was demonstrated in all patients.⁽³¹⁾

Dose-dependent respiratory depression may be seen in children following the administration of epidural opioids in doses exceeding 0.05 mg/kg.⁽³²⁾ In a study of children undergoing cardiac surgery and receiving epidural morphine in a bolus dose of 0.05 mg/kg followed by a continuous infusion, however, respiratory depression did not occur.⁽²¹⁾ Several other studies in children have shown excellent analgesia and no evidence of respiratory depression when the dose of epidural morphine does not exceed 0.05 mg/kg.^(33,34,35)

Similarly, doses of intrathecal morphine of 0.02 or 0.03 mg/kg may result in significant respiratory depression following cardiac surgery in children.⁽²⁰⁾ Intrathecal morphine 0.01 mg/kg has also been associated with respiratory depression postoperatively when combined with intravenous fentanyl 0.02 mg/kg and midazolam in adult patients undergoing cardiac surgery.⁽³⁶⁾ However, in a review of children given intrathecal morphine in a dose of 0.02 mg/kg in whom no intravenous opioids were administered during surgery, no patient had postoperative respiratory depression.⁽³⁷⁾ In addition, no child required supplemental opioid analgesia for at least 15 hours following surgery. In a recent study comparing intrathecal morphine in doses of 0.005, 0.007, and 0.010 mg/kg in children having open heart surgery, the trachea of each patient was extubated at the conclusion of surgery and no patient had signs of respiratory depression.⁽³⁸⁾

Epidural hematoma formation following epidural or spinal anesthesia is a rare but potentially catastrophic complication of neuraxial blockade in patients receiving anticoagulant therapy. In an analysis of 20 series, including more than 850,000 cases of epidural blockade and 650,000 cases of spinal anesthesia in adult patients, only 3 case reports of epidural hematoma were documented.⁽³⁹⁾ Based on these data, the author estimated the risk of epidural hematoma following epidural anesthesia to be 1:150,000, and 1:220,000 following spinal anesthesia. Unfortunately, it is unknown what the incidence of clotting disorders, use of anticoagulants, or traumatic procedures was in these reports.

In a thorough review of the literature from 1906 through 1994, Vandermeulen et al., found 61 published cases of epidural or subdural hematoma following epidural or spinal anesthesia in adult patients.⁽⁴⁰⁾ Of these 61 cases, 42 occurred in patients with impaired coagulation prior to epidural or spinal needle placement, including 25 patients receiving heparin. In 15 patients, the procedure was reported to be difficult and/or traumatic. A clotting disorder or difficult/traumatic needle placement was present in 53 of the 61 cases (87%).

In a series of over 4,000 epidural or spinal anesthetics performed prior to anticoagulation with heparin for vascular surgery, no cases of epidural hematoma were reported.⁽⁴¹⁾ The authors reported important precautions which were undertaken in these patients, including delaying surgery for 24 hours in the event of traumatic needle placement and allowing at least 60 minutes between needle placement and heparin administration. Other recommended precautions include use of the smallest dose of heparin necessary to achieve therapeutic objectives and removal of epidural catheters only when normal coagulation function has been restored.⁽⁴²⁾ Epidural hematoma formation has not been reported in a patient following spinal or epidural anesthesia prior to cardiopulmonary bypass.

Regional Anesthesia Techniques

A variety of techniques of neuraxial blockade have been reported in children undergoing cardiac surgery. These include intrathecal (spinal) and epidural techniques utilizing opioids and/or local anesthetics. Epidural approaches include single dose ("single shot") caudals as well as thoracic, lumbar, and caudal catheter techniques.

Intrathecal (Spinal) Techniques

The use of spinal opioid analgesia as an adjunct to general anesthesia was first described by Mathews and Abrams in 1980.⁽⁴³⁾ In this report, 40 adults received intrathecal morphine in a dose of 1.5–4.0 mg prior to surgery. All patients remained comfortable for more than 24 hours. Subsequently, many studies demonstrated the efficacy of spinal opioids, primarily morphine, in producing analgesia following cardiac surgery in adult patients. These reports have been summarized elsewhere.⁽⁴²⁾ Although intrathecal morphine alone has not been shown to attenuate the stress response associated with cardiac surgery per se, it may attenuate the stress response in the immediate postoperative period.⁽⁴⁴⁾

In order to augment the effects of intrathecal opioids in reducing the stress response and circulatory instability in

patients undergoing cardiac surgery, local anesthetics have been used in combination with intrathecal opioids. In adults, however, intrathecal injection of local anesthetics in doses needed to attain high spinal blockade results in hypotension.⁽⁴⁵⁾ Children, on the other hand, do not develop hypotension following high spinal blockade. Finkel, et al., studied the hemodynamic effects of spinal anesthesia in children undergoing cardiac surgery.⁽³¹⁾ In this study, 30 children between the ages of 7 months and 13 years received intrathecal morphine mixed with tetracaine following induction of general anesthesia and tracheal intubation. The dose of tetracaine was adjusted for age, according to the estimated volume of cerebrospinal fluid. Patients aged 6–12 months received intrathecal tetracaine 2.0 mg/kg, those between the ages of 1 and 3 years received 1.0 mg/kg, and those over the age of 4 years received 0.5 mg/kg. Tetracaine was mixed with 10% dextrose to yield a 0.5% hyperbaric solution, and all patients received preservative-free morphine in a dose of 0.005–0.010 mg/kg. Patients were placed in a 30° head-down (Trendelenberg) position for a minimum of 10 minutes following administration of the intrathecal solution. Although there was mild slowing of the heart rate in children over age 4 years, there was no clinically significant bradycardia nor hypotension observed. Hammer et al., have also reported hemodynamic stability following intrathecal tetracaine/morphine in children undergoing cardiac surgery.⁽⁴⁶⁾

We currently utilize spinal anesthesia in combination with general anesthesia in children for whom tracheal extubation is planned prior to leaving the operating room following open heart surgery. Surgical procedures include, for example, repair of atrial and/or ventricular septal defects or partial anomalous pulmonary venous return, aortic or pulmonary valvuloplasty, right ventricular-to-pulmonary artery conduit placement or exchange, bidirectional cavopulmonary shunt, and the modified Fontan procedure. Spinal anesthetic blocks (SAB) are performed immediately after tracheal intubation (i.e. prior to placement of arterial and central venous catheters) in order to maximize the time interval between SAB and heparinization for cardiopulmonary bypass. Patients are placed with the head of the table 30° down for a minimum of 15 minutes following SAB. No intravenous opioids are administered intraoperatively. Our dosing regimen for SAB is based on the above-referenced studies and is shown in Table 1.

Table 1. Dosing regimens for spinal anesthesia.

Age (years)	Tetracaine (mg/kg)	Morphine (μ g/kg)
< 1	2.0	7
1–3	1.0	7
4–8	0.5	7
>8	0	10

Epidural Techniques

The use of postoperative epidural analgesia in patients undergoing open heart surgery was first described by Hoar et al., in 1976.⁽⁴⁷⁾ Subsequently, El-Baz and Goldin reported the use of epidural blockade initiated prior to surgical incision.⁽⁴⁸⁾ In 1989, Rosen and Rosen first reported the efficacy of epidural morphine analgesia in children undergoing cardiac surgery.⁽²²⁾ Since then, many studies have reported favorable results with epidural anesthesia and analgesia for cardiac surgery.⁽⁴²⁾

In general, epidural anesthesia is used in patients undergoing open heart surgery for whom tracheal extubation is planned in the OR following the completion of surgery or shortly thereafter. The epidural technique most commonly used in children appears to be the administration of a single dose of morphine injected into the caudal epidural space. Morphine is favored for caudal epidural administration due its low lipid solubility and commensurate tendency to spread rostrally to thoracic dermatomes.^(49,50) Following induction of general anesthesia and tracheal intubation, preservative-free morphine sulfate is injected in a dose of 0.05–0.10 mg/kg into the caudal epidural space via an epidural needle or intravenous catheter. Intravenous opioids, if administered intraoperatively, are given in restricted doses (eg., fentanyl 0.01–0.02 mg/kg).

Alternatively, a caudal epidural catheter may be inserted to facilitate continuous administration of morphine during and after surgery. Following an initial dose of epidural morphine 0.04 mg/kg, a continuous infusion is begun in a dose of 0.0075 mg/kg/hr. The infusion is continued throughout the intraoperative period and maintained postoperatively for 48–72 hours. If the patient appears overly somnolent the infusion is decreased in increments of 0.0025 mg/kg/hr.¹

In order to attenuate the stress response associated with cardiac surgery and cardiopulmonary bypass as well as optimize postoperative analgesia, a combination of epidural opioids and local anesthetic agents may be used. Although local anesthetic agents may spread to thoracic dermatomes when administered via the caudal epidural space, potentially toxic doses of local anesthetics may be required to achieve thoracic analgesia.^(51,52) Thoracic epidural blockade may be achieved with greater safety and efficacy by placing the epidural catheter tip in proximity to the spinal segment associated with surgical incision. Segmental anesthesia may then be achieved with lower doses of local anesthetic than those needed when the catheter tip is distant from the surgical site. In infants, a catheter can reliably be advanced from the caudal to the thoracic epidural space.⁽⁵³⁾ For example, with the infant in the lateral decubitus position, a 20-gauge epidural catheter may be inserted via an epidural needle or an 18-gauge intravenous catheter placed through the sacrococcygeal membrane and advanced 16–18 cm to the mid-thoracic epidural space. Minor resistance to passage of the catheter may be overcome by simple flexion or extension of the spine. If continued resistance is encountered, no attempt should be made to advance the catheter further, as the catheter may become coiled within or exit the epidural space. In older children, a thoracic epidural catheter may be inserted directly between T4 and T8 to provide intraoperative anesthesia and postoperative analgesia. As with SAB, epidural catheter placement should be performed immediately following tracheal intubation in order to maximize the time elapsed prior to heparin administration for CPB. In our practice, an initial dose of hydromorphone 0.007–0.008 mg/kg and 0.25% bupivacaine 0.5 ml/kg is administered. Subsequent doses of 0.25% bupivacaine 0.3 ml/kg are administered intraoperatively at approximately 90 minute intervals. No intravenous opioids are given during surgery. Postoperatively, a continuous infusion of 0.10% bupivacaine and hydromorphone 0.003 mg/ml is administered at a rate of 0.3 ml/kg/hr. An advantage of epidural catheter compared with “single shot” techniques is that adjustments can be made in dosing postoperatively according to the patient’s level of comfort. For example, a “bolus” of epidural anesthetic agents may be given and the infusion rate increased if the patient is experiencing pain. Alternatively, the infusion may be decreased if the patient becomes somnolent. Our dosing regimen for thoracic epidural anesthesia and analgesia is shown in Table 2.

Table 2. Dosing regimens for epidural anesthesia.

Intraoperative Dosage		Postoperative Infusion
Bupiv. 0.25% (ml/kg)	HM (μg/kg)	
0.5 initially, then 0.3 q 90 min.	7–8	Bupiv 0.1%+HM 3 μg/ml @ 3 ml/hr

Bupiv. = bupivacaine; HM = hydromorphone

Treatment of Side Effects

Side effects related to neuraxial opioids include nausea and vomiting, pruritus, somnolence, respiratory depression, and urinary retention. Nausea and vomiting as well as pruritus appear to be relatively uncommon in infants and are primarily seen in children over the age of 3 years. These side effects are more common with morphine compared with hydromorphone and fentanyl.⁽⁵⁴⁾ Due to greater rostral spread, respiratory depression is also more common when morphine is used compared with hydromorphone.^(49,54) Urinary retention is seen most commonly during the initial 24 hours of therapy, during which time the majority of patients have urinary catheters in place. Suggested treatment for side effects related to spinal and epidural opioids is shown in Table 3.

¹D. Rosen – personal communication

Table 3. Treatment for side effects of neuraxial opioid administration.

Side effect	Treatment	Comments
Nausea/vomiting	<p>Metoclopramide (Reglan[®]) 0.1–0.2 mg/kg/dose IV Q 6 hours Maximum dose: 10 mg</p> <p>Droperidol (Inapsine[®]) 0.025–0/05 mg/kg IV Q 6 hours prn Maximum dose: 1.25 mg</p> <p>Diphenhydramine (Benadryl[®]) 0.5–1.0 mg/kg IV Q 6 hours prn Maximum dose: 50 mg</p> <p>Ondansetron (Zofran[®]) 0.1–0.2 mg/kg IV Q 6 hours prn Maximum dose: 4 mg</p> <p>Nalbuphine (Nubain[®]) 0.1 mg/kg IV Q 6 hours prn</p> <p>Naloxone (Narcan[®]) 0.001–0.005 mg/kg/hr infusion</p> <p>Propofol (Diprivan[®]) 0.001–0.010 mg/kg hr infusion</p>	<p>Extrapyramidal reactions may occur but are uncommon</p> <p>Very sedating – avoid if somnolent</p> <p>Very sedating – avoid if somnolent</p> <p>May substitute other 5-HT₃ antagonist, eg. Granisetron (Kytril[®])</p> <p>Excessive doses may compromise analgesia</p>
Pruritus	<p>Diphenhydramine (Benadryl[®]) 0.5–1.0 mg/kg IV Q 6 hours prn Maximum dose: 50 mg</p> <p>Nalbuphine (Nubain[®]) 0.1 mg/kg IV Q 6 hours prn</p> <p>Naloxone (Narcan[®]) 0.001–0.005 mg/kg/hr infusion</p>	<p>Very sedating – avoid if somnolent</p> <p>Excessive doses may compromise analgesia</p>
Somnolence	<p>Decrease epidural opioid infusion</p> <p>Consider low-dose naloxone infusion (above)</p>	
Respiratory depression	<p>Severe: Administer 100% via facemask Initiate positive pressure ventilation prn Naloxone 0.001–0.010 mg/kg IV Stop epidural infusion</p> <p>Subsequently/Mild-moderate depression: Increase FIO₂ Reduce epidural opioid infusion Naloxone (Narcan[®]) 0.001–0.005 mg/kg/hr infusion</p>	
Urinary retention	<p>Replace urinary catheter prn</p>	

Conclusion

The use of epidural and spinal anesthesia in infants and children may attenuate the stress response and thereby decrease morbidity and mortality associated with cardiac surgery. In addition, the use of these regional anesthesia techniques during and after cardiac surgery may result in improved pulmonary function, greater circulatory stability, and better postoperative pain control compared with general anesthesia and postoperative intravenous opioid analgesia. To the extent that regional anesthesia may facilitate tracheal extubation in the operating room immediately following surgery, complications and the expense associated with mechanical ventilation in the postoperative period may be avoided. In those patients who undergo tracheal extubation in the ICU, cost savings may be achieved due to reductions in time of mechanical ventilation and ICU length of stay, as well as earlier resumption of a regular diet.

The risks of epidural and spinal anesthesia in these patients include undesired side effects (nausea and vomiting, pruritus), hypotension, respiratory depression, and epidural hematoma formation. The incidence of side effects does not appear to exceed that associated with intravenous opioid analgesia. Hypotension, associated with local anesthetic spinal and epidural blockade in adult patients, is uncommon in infants and young children. Postoperative respiratory depression is greatly reduced by avoiding intraoperative opioids and using prudent doses of spinal and epidural opioids.

The risk of epidural hematoma formation is small but finite. This risk can be minimized by employing reasonable safeguards. Appropriate precautions include selecting patients with normal coagulation function prior to needle placement, abandoning the regional anesthesia technique if needle placement is difficult, and delaying surgery in the event of return of blood via the needle or epidural catheter. The time interval between needle placement and heparin administration should be maximized, allowing for an interval of at least 60 minutes. Epidural catheters should be removed only after normal coagulation function has been restored.

Future studies may provide additional information regarding the dose-response relationships of regional anesthetic agents in patients undergoing cardiac surgery. Modulation of the stress response in neonates, e.g. utilizing total spinal anesthesia, warrants investigation. In addition, strategies to decrease the incidence of side-effects (e.g. prophylactic antiemetic therapy) may be developed.

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