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Invited Commentary

Intrathecal Morphine for Minimally Invasive Cardiac Surgery: The Next Frontier for Cardiac Anesthesia Care?

Pain control is an important aspect of postoperative recovery for patients undergoing cardiac surgical procedures. There is a concerted effort toward developing multimodal pain treatments in order to decrease reliance solely on intravenous opioids. With minimally invasive cardiac surgery, there is an expectation of expeditious patient recovery. Effective pain treatment protocols are essential and must address the significant discomfort resulting from surgical incisions, tissue retraction, and chest tube placement. Given the importance of alternative methods for postoperative analgesia in patients undergoing minimally invasive cardiac surgery, a randomized, placebo-controlled, and double-blinded clinical trial by Dhawan et al[1] highlighted this next frontier in postcardiac surgery analgesia. The authors demonstrated that intrathecal morphine administered prior to totally endoscopic coronary artery bypass decreased postoperative opioid dosage.

Based on these findings, Trela and Dhawan presented 2 cases highlighting the use of intrathecal morphine in minimally invasive cardiac surgery in the current issue of the *Journal of Cardiothoracic and Vascular Anesthesia*. The authors described the administration of 5 μg/kg of intrathecal morphine in 2 patients undergoing robotic totally endoscopic cardiac procedures—coronary artery bypass and myocardial bridge unroofing. Postsurgical recovery was improved by the addition of this pain treatment modality, and patients were discharged from the hospital 2 days after their surgical procedures.

An important question stemming from this report is the dosing of intrathecal morphine. The authors chose to dose intrathecal morphine at 5 μg/kg because prior studies suggested that this dose strikes a balance between postoperative pain control and adverse effects.[1,2] However, dose-response studies have not yet been performed in the setting of minimally invasive cardiac surgery. It is possible that doses lower than 5 μg/kg could be effective, so an investigation as to the ED90 of intrathecal morphine in this population would be helpful in decreasing the risk of adverse respiratory effects. Such an approach has been used in obstetric anesthesia, in which commonly used doses of intrathecal morphine were initially quite high but have since been decreased and optimized with the publication of dose-response studies.[3]

Postoperative monitoring for respiratory depression of patients who receive intrathecal morphine is important. The duration of action of intrathecal morphine follows a biphasic pattern. This results in respiratory depression 1-to-2 hours after administration and, subsequently, 6-to-18 hours after intrathecal morphine treatment.[4,5] The American Society of Regional Anesthesia and Pain Medicine (ASRA) published guidelines in 2009 that recommended respiratory rate monitoring every hour for the first 12 hours and every 2 hours for the next 12 hours for healthy obstetric patients receiving intrathecal morphine.[6] Given that patients undergoing cardiac surgery recover in an intensive care unit, this level of monitoring should be attainable. However, as there is continued pressure to decrease length of stay and discharge patients earlier from the intensive care unit, it will be important to remember that these patients should have close monitoring for respiratory depression after intrathecal morphine injection. Multidisciplinary planning with perioperative pain evaluation and treatment must be in place to ensure patient safety and treatment satisfaction.

Another consideration for the administration of intrathecal morphine is the risk of spinal hematoma with procedural heparinization. The ASRA guidelines from 2018 recommended that intravenous heparin should be administered no earlier than 1 hour after neuraxial procedures, although there are insufficient data specifically with regard to cardiac surgery.[7] Clinicians should be careful to document the time of intrathecal morphine administration so as to not administer the heparin too early should the surgical procedure proceed expeditiously.

The duration of analgesia from intrathecal morphine is up to 24 hours.[8] It is important to remember, however, that the patient experience of pain begins after emergence from anesthesia. Given that the time between when intrathecal morphine

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is administered preoperatively and the patient emergence from general anesthesia can be several hours, the patient's experience of analgesia is shortened. Is there a role for postoperative intrathecal morphine administration? Certainly, postoperative administration would result in a "longer" duration of analgesia. At the same time, the ASRA guidelines on regional anesthesia in patients receiving antithrombotic therapy recommend waiting 4-to-6 hours after administration of heparin and verifying a normal coagulation status prior to performing a neuraxial technique.[7] Thus, the balance between when to place intrathecal morphine and the risks of spinal hematoma must be determined based on the use of anticoagulation for the procedure.

The use of intrathecal morphine is important because it may help to decrease the incidence of persistent postoperative pain syndrome. Uncontrolled acute postoperative pain is associated with an increased risk for persistent postoperative pain syndrome.[9,10] Chronic postsurgical pain is characterized as pain symptoms reported 3 months after surgery.[11] A meta-analysis of 23 studies with more than 11,000 cardiac surgical patients showed that 37% of patients developed persistent postoperative pain during the initial 6-month postoperative period, and up to 17% of patients had symptoms of persistent postoperative pain 2 years after surgery.[9] If such a large percentage of patients continue to experience persistent postoperative pain, this may lead to an increased risk of prescription opioid use with the potential for addiction. Brown et al[12] completed a retrospective analysis of more than 35,000 cardiac surgical patients, and demonstrated that nearly 1 out of 10 opioid-naïve patients continued to use opioids more than 3 months after cardiac surgery. Therefore, intrathecal morphine may be a novel way to decrease the risk of persistent postoperative pain syndrome and addiction in society as a whole.

There remains the question of the application of this technique in high-risk patients. The intrathecal morphine dosage was based on the randomized study by Dhawan et al,[1] which excluded patients with obstructive sleep apnea and morbid obesity. As the complexity of patients undergoing minimally invasive cardiac surgery increases, there is a need for additional data on appropriate intrathecal morphine dosing to maximize pain control while decreasing the side effect profile, including respiratory depression leading to increased risk of postoperative mechanical ventilation. There is also an assumption that patients undergoing minimally invasive cardiac surgery are opioid-naïve. It would be interesting to take into account patients' baseline morphine-equivalent intake when adjusting intrathecal morphine dose.

In conclusion, the use of intrathecal morphine for postoperative analgesia in minimally invasive cardiac surgery is a clinically relevant concept that warrants further investigation and clinical application. It is still unknown what dose might be ideal and, as such, dose-response studies will be particularly helpful in finding a dose from which the clinical effect is balanced with the risks of adverse effects. Simultaneously, the timing of intrathecal morphine administration is an important consideration, as the risks of spinal hematoma are highest when heparin is administered in short order. Intrathecal morphine for postoperative analgesia in minimally invasive cardiac surgery is an important new frontier for cardiac anesthesia.

Conflict of Interest

None.

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