Intrathecal morphine in two patients undergoing deep hypothermic circulatory arrest during aortic surgery -A case report-

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We retrospectively report the first use of intrathecal morphine prior to incision in two male patients undergoing a complex aortic reconstruction, who required complete circulatory arrest under deep hypothermia for intraoperative and postoperative pain control. We administered intrathecal morphine to two male patients undergoing circulatory arrest and deep hypothermia. Patients were fully heparinized prior to cardiopulmonary bypass. Deep hypothermic circulatory arrest was performed by cooling the patients to 18°C. Following the surgery, the neurologic status was monitored. The management of postoperative pain is a quality standard in health care. During the first 24 hours after surgery, we observed excellent analgesia without the associated side effects, thus, reducing the time required for pain control by the nursing staff. A successful analgetic strategy not only enhances the patient satisfaction, but may improve the postoperative outcome. However, complications, such as increased risk of epidural hematoma formation, are of special concern in cardiac surgery. (Korean J Anesthesiol 2012; 63: 563-566)

Key Words: Cardiac surgical procedures, Circulatory arrest (hypothermia induced), Morphine, Spinal anesthesia.

The management of postoperative pain is monitored as a quality standard in healthcare [1]. Cardiac surgery is associated with intense postoperative pain. A successful analgesic strategy will not only enhance patient satisfaction, but may also improve postoperative outcome and decrease the nursing time for analgesia. Pain significantly impairs multiple organ function, and has been shown to adversely affect the sympathetic, hemodynamic, hemostatic, respiratory, and hormonal responses, among others [2-4]. The associated combination of increased myocardial oxygen consumption and vasoconstriction, altered hemostasis and hypercoagulability, inflammation, and impaired respiratory function are especially detrimental in cardiac surgery patients. The postoperative course of these patients can be complicated by myocardial

infarction, arrhythmias, coronary artery bypass graft occlusion, hemorrhage, and renal and respiratory failure [5]. Various approaches are used to address the postoperative pain in this patient population. Intravenous narcotic administration is the most commonly used technique [6]. Intrathecal and epidural techniques are promising techniques to consider, and can provide extensive pain relief [7]. However, concerns for complications, such as the increased risk of epidural hematoma formation, are of special interest in cardiac surgery patients subjected to hypothermia and anticoagulation intraoperatively or during the postoperative period [8].

We describe the first use of intrathecal morphine in two patients undergoing deep hypothermic circulatory arrest for complex aortic root reconstructions.

Case Report

Two male patients were scheduled for reconstruction of their aneurysmal aortic roots. The intraoperative and postoperative management along with the clinical course are detailed in Table 1. These case reports are presented retrospectively; informed consent was obtained from these patients prior to all interventions. Approval to report the cases was received from the University of Florida Institutional Review Board, and obtaining informed consent for this report was waived.

On the day of surgery, our patients had standard monitors and an arterial catheter was placed. Under sterile conditions, while in a sitting position, intrathecal preservative-free morphine was injected via the L2-3 interspace midline approach, using a 27-gauge Whitacre and introducer needle (Table 1).

Each patient was then transported to the operating room and after reapplication of monitors, vital sign assessment and preoxygenation anesthesia was induced with propofol and neuromuscular blockade. Isoflurane and neuromuscular blockade were used for maintenance. A pulmonary artery catheter and transesophageal echoprobe were inserted, and bispectral monitoring, capnography, and cerebral oximetry were established. In addition, cardiac indices, blood gases, coagulation (ACT, INR, aPTT, TEG), neuromuscular blockade, temperature (esophageal, bladder, rectal), and urine output were monitored in the standard fashion.

Patients were fully heparinized prior to cardiopulmonary bypass. Deep hypothermic circulatory arrest was performed by cooling the patients to 18°C and placing the head in an ice cap. An isoelectric EEG was induced with etomidate titrated to effect. Both patients were placed in the Trendelenburg position. After rewarming and obtaining adequate indices, cardiopulmonary bypass was discontinued, and protamine was administered for heparin reversal (ACT at baseline prior to heparinization). Once the patients' hemodynamics and coagulation were stable in the operating room, they were awakened for a neurologic examination and then re-sedated with propofol. Our patients remained intubated in the intensive care unit (ICU) until immediate surgical complications, such as hemorrhage, were excluded. A propofol infusion was used for patient comfort while intubated, and was titrated to allow the patients to interact. Additional pain medication was given at the discretion of the ICU provider. Extubation, oral intake, and ambulation were determined by the ICU provider or cardiac surgeon.

Table 1. Clinical Characteristics and Course

Observation	Patient 1	Patient 2
Age (yr)	51	63
Height (cm)	183	188
Weight (kg)	111	94
Intrathecal morphine (mg)	0.7	0.6
Intraoperative narcotics	None	100 µg fentanyl intravenously
Intravenous morphine (mg)-first 24 hr	0	0
Intravenous morphine (mg)-first 48 hr	2	2
Oral narcotics after 24 hr	Acetaminophen and oxycodone	Acetaminophen and oxycodone
Time from intrathecal morphine to heparin (min)	120	180
Maximal activated clotting time (sec)	931	1,500
Lowest body temperature intraoperatively (°C)	18	18
Time for circulatory arrest (min)	15	56
Admission SICU: INR*/aPTT[†]/platelets[‡]	1.4/32 s/163 (×10⁹/L)	1.9/31 s/170 (×10⁹/L)
24 hr SICU: INR*/aPTT[†]/platelets[‡]	1.4/34 s/160 (×10⁹/L)	1.4/30 s/171 (×10⁹/L)
Time from SICU admission to extubation (hr)	12	6
Time to oral intake after extubation (hr)	1	3
Time after SICU admission to ambulation (hr)	14	20
Discharge from SICU	POD 2	POD 2

SICU: surgical intensive care unit, INR: international normalized ratio, aPTT: activated plasma thromboplastin time, POD: postoperative day. *Normal range 0.8−1.2, [†]Normal range: 25−39 seconds, [‡]Normal range 150−450 (×10⁹/L).

Discussion

Studies have shown that a high-dose narcotic regimen does not affect the systemic stress response to surgery [7]. These findings led to an increasing interest in the use of neuraxial techniques, such as intrathecal or epidural drug administration. Indeed, local anesthetics and narcotics delivered to the neuraxis are able to attenuate the stress response after cardiac surgery [8]. A prospective randomized study of patients undergoing coronary artery bypass grafting showed significantly better outcomes in regards to supraventricular arrhythmias, respiratory infection, renal failure, and confusion in patients who received a thoracic epidural infusion of bupivacaine and clonidine, compared to that of the control group, who received a general anesthetic and intravenous narcotics [9]. However, that study had some limitations, one being that beta-blockers were allowed. Another study by Priestly et al. [10] found improved pain scores and enhanced early extubation, but no effects on arrhythmias, hospital discharge, or overall outcome. Nonetheless, both studies provide strong evidence that excellent analgesia can be provided by an epidural technique, even allowing for performing cardiac surgery in awake, nonintubated patients [11].

In our estimation, a significant limitation of the epidural technique is that a catheter has to be placed in patients who are scheduled to receive high-dose heparin, may require immediate postoperative anticoagulation, and could be subject to major alterations of their hemostatic system. Thereby, it increases the risk of epidural hematoma formation, which could result in paraplegia.

The intrathecal single-shot administration of drugs, such as morphine, offers an elegant alternative in these patients, making catheter placement unnecessary and reducing the risk of hematoma formation [12]. Furthermore, both intrathecal and epidural narcotic administration are equal in analgesic potency [8]. This rationale - to use the intrathecal route - proved effective in our patients who were undergoing a complex aortic root reconstruction using cardiopulmonary bypass and circulatory arrest under deep hypothermia, which requires full heparinization. Additionally, given the extracorporeal circulation and deep hypothermia, major changes in their hemostatic system and an exaggerated stress response were expected.

Intrathecal morphine has been extensively studied in cardiac surgery patients, and no reports of spinal hematoma, to our knowledge, have been reported [8]. As in our patients, the majority of published studies have used full heparinization, but with only mild hypothermia ($28-32^{\circ}C$) and no circulatory arrest. A trial of intrathecal morphine in patients undergoing deep hypothermic cardiac arrest has not been reported, and

we can only speculate that concerns regarding the possibility of developing a spinal hematoma may have played a role. Statistically, the risk of a spinal hematoma following a dural puncture is 1 : 220,000 [12]. The strategy we implemented, the avoiding of full heparinization within two hours after dural puncture, abandoning the puncture if more than three attempts are necessary, and postponing the surgery for 24 hours if a traumatic puncture occurred, is compliant with the literature [8]. The potential necessity to postpone surgery should be discussed and agreed upon by the patient and the surgeon before proceeding with an intrathecal approach.

In both of our cases, we are able to attest to the intense and lasting analgesia of intrathecal morphine, as neither of our patients requested narcotics during the first 24 hours of the postoperative period (Table 1). This finding is remarkable even further, as we did not administer supplemental narcotics during surgery in the first patient and only 100 µg of fentanyl in the second patient. Narcotic administration intraoperatively was commonly performed in other studies. In addition, administration of narcotics in the postoperative period was left completely up to the ICU provider, and was not influenced by the anesthesia team. Other studies reported morphine consumption of 21.3 mg in the control group versus 13.6 or 11.7 mg in patients receiving intrathecal morphine [13]. Side effects, such as pruritus, which can be severe in up to 1% and mild in up to 30% of patients receiving intrathecal morphine [8], were not observed in our two patients.

We did not assess the effects of intrathecal morphine on the return of function in our two cases, as our investigation was preliminary, but we can state that both of our patients were extubated, ambulating or sitting, and successfully started on oral intake within 24 hours after admission to the ICU (Table 1). Studies are inconclusive with regard to improved functional outcome after intrathecal morphine administration. There was no improvement in pulmonary function; however, improvement in the airway clearance and coughing, and ambulation was noted [14]. Overall, the medical literature persistently shows a clear benefit of intrathecal morphine in providing excellent and lasting analgesia.

In summary, the two cases we have presented with the use of intrathecal morphine, for the first time, in patients undergoing circulatory arrest and deep hypothermia, we observed high quality analgesia without associated side effects. Precautions with regard to the risk of hematoma formation, however, have to be followed in these types of patients.

Acknowledgments

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