Potential Beneficial Effects Of Intrathecal Opioids In Cardiac Surgical Patients

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Citation

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Abstract

Background: Postoperative pain control plays an important role on prognosis of patients undergoing thoracic surgery. The length of stay in the intensive care units and hospital is correlated with the quality of pain management. We assessed the potential role of intrathecal opioid supplement for fast tracking cardiac surgery patients.

Methods: This is a retrospective, chart review of 133 consecutive patients undergoing open-heart procedure at Buffalo VA Medical Center. They were studied with respect to time-to-extubation, the degree of pain relief, and postoperative parentral narcotic use. Sixty-four patients received supplemental intrathecal opioids and 69 patients received conventional opioid-based anesthesia. Postoperative visual analog pain scores and 24 h analgesic requirements were measured as indices of postoperative pain. Time to extubation, partial pressure of oxygen and carbon dioxide were measured as indices of respiratory function.

Results: Patients receiving intrathecal opioids appeared to be more comfortable (VAS = 2 vs. 7) upon arrival at the surgical intensive care unit (SICU) and 24 h after surgery (VAS = 3 vs. 5). These patients also required less parentral morphine in the first 24 hours after surgery (11.4 ± 3.1-mg vs. 52.6 ± 6.2; $p<0.05$). The majority of patients receiving intrathecal opioids were extubated in the operating room following termination of surgery, suggesting a lower incidence of postoperative respiratory depression. This was associated with a lower need for reintubation that those receiving IV opioids.

Conclusion: We believe that the addition of spinal opioids was beneficial in the early postoperative care of cardiac surgery patients with respect to pain management and ventilatory requirements.

INTRODUCTION

Undertreated surgical pain prolongs recovery and may result in multisystem complications ([1,2,3,4]). Effective coughing and deep breathing are major factors required for weaning from mechanical ventilation, extubation, the prevention of atelectasis, and the possibility of pneumonia in patients undergoing thoracic surgical procedures. Adequate pain control is essential to this process ([5]). Epidural infusion of opioids along with dilute concentrations of local anesthetic agents has been very effective in decreasing post-thoracotomy pain and related complications ([6,7,8]). However, because of the risk of peridural hematoma secondary to systemic anticoagulation in these patients, anesthesiologists are reluctant to place epidural catheters ([9]). The recent interest in rapid recovery and early ambulation of patients ("fast-tracking") after cardiac surgery has prompted investigations into the use of neuraxial analgesia for these procedures ([10,11]).

With the advent of an updated cardiothoracic program at the Buffalo VA Medical Center, the anesthesia service was requested to "standardize" an anesthetic regimen to minimize the variability of anesthesia care. Our approach was to initiate a common practice protocol for patients undergoing all cardiac surgeries that we thought would be beneficial with respect to postoperative pain control, as well as minimize requirements for postoperative ventilatory support. We initially hypothesized that an intrathecal injection of less lipid soluble agents such as morphine, combined with a faster-acting opioid of shorter duration, might allow good postoperative pain control ([12,13]). We also hypothesized that adequate analgesia during surgery and the immediate postoperative period would enable these patients to be rapidly weaned from ventilatory support (11,13) and possibly improve pulmonary gas exchange.

This retrospective analysis of our patients describes the effects of a single intrathecal injection of opioids on the recovery of patients undergoing cardiac surgical procedures. The quality of analgesia, time to extubation, pulmonary function, intensive care unit (ICU), and hospital stays were examined in the group receiving intrathecal (IT) narcotics, and compared to a group treated conventionally with intravenous (IV) opioid analgesics in the perioperative period.

METHODS

One hundred thirty three patients undergoing cardiac surgical procedures during a twelve month period (September 1997- August 1998) at the Western New York VA Healthcare System (Buffalo VAMC) were studied retrospectively. Sixty-four patients had received intrathecal narcotics (IT) during this period as part of their anesthesia care. In 69 patients, no intrathecal drug was administered prior to cardiac surgery and intraoperative analgesia was provided using intravenous narcotics; all patients received general anesthesia. Patients undergoing cardiac surgery through a median sternatomy incision, with and without cardiopulmonary bypass circulation, were included. Patients that were excluded from the study were those that had been brought back to the operating room within 24 hours, patients with recent neurological events (< 1 month old), and patients for whom coronary artery bypass grafting (CABG) was not being performed for the first time. The IT group included patients that were therapeutically anticoagulated prior to surgery, but did not have heparin infusing upon arrival in the operating room, nor for three hours prior to that time. The IV group included similar patients, but also all patients requiring anticoagulation up to the time of surgery were placed in this group. ASA physical Status, New York Heart Association (NYHA) classification for functional state, and the Canadian Cardiovascular Society (CCS) classification for the state of angina were recorded.

Preoperative evaluation had included a personal interview, physical examination, and oral administration of an intermediate-acting benzodiazepine (lorazepam, 2 mg the night prior to surgery).

Upon arrival at the operating room, patients received a dose of midazolam (2 mg IV). Routine non-invasive monitors were placed and supplemental oxygen was provided. Patients in the IT group were positioned in the sitting or lateral position, following epidermal infiltration of local anesthetic agent (lidocaine 1 %). A 22 gauge Quinke spinal needle was introduced into the L2-L3, or L3-L4 interspace, and advanced into the spinal space, as confirmed by the free flow of cerebrospinal fluid. Preservative-free morphine (0.007 mg/kg) mixed with fentanyl (1.5 µg/kg) were then injected. Following the injection of intrathecal opioids, the patient resumed the supine position and a radial arterial line was placed. Both groups of patients were induced using etomidate (0.2-0.3 mg/kg) and endotracheal intubation was facilitated by administration of cis-atracurium (0.25 mg/kg). The IT group received fentanyl 2 µg-kg as part of the induction regimen; the IV group received fentanyl, 4 m g/kg. Pulmonary artery catheters were placed in a routine fashion through the right internal jugular vein. Anesthesia was maintained with sevoflurane (1-2 MAC). For “light anesthesia”, hypertension and/or tachycardia were treated initially with increases of sevoflurane until 2 MAC was reached when supplemental boluses of fentanyl, 2 µg/kg, were used as required, at the discretion of the attending anesthesiologist. “Deep anesthesia” was treated by lowering the inhalation anesthetic concentration by 50%, initially, followed by fluid therapy and boluses of phenylephrine as required. The objective, during maintenance, was to maintain heart rate and blood pressure within 25% of preoperative values. During cardiopulmonary bypass, an infusion of propofol (75-100 µg/kg/min) was used to maintain anesthesia. Throughout surgery, muscle relaxation was maintained at or below one of four twitches in the train-of-four paradigm. Following closure of the chest, no further muscle relaxant was administered, and mechanical ventilation was resumed using an FiO2 adequate to maintain arterial oxygen saturation above 95%. The patients were extubated in the operating room, at the discretion of the attending anesthesiologist and attending surgeon , if they were spontaneously ventilating with tidal volume > 5 cc/kg, had an end-tidal CO2 of < 55 and a respiratory rate of < 30, were hemodynamically stable, not actively bleeding, and could squeeze our hands firmly. Those patients who did not meet these extubation criteria were transferred to the ICU, placed on a ventilator and subsequently weaned as per ICU protocol. The time to extubation was recorded in a fraction of an hour from the time of arrival. One hour after extubation arterial blood gas samples were analyzed for PaO2 and PaCO2 and bicarbonate ion.

Table 1: Extubation Criteria in the Operating Room

- Responding to verbal command
- Absence of active bleeding

- Hemodynamic stability
- Normothermia (Core temperature >35.8 °C)
- Complete reversal of residual muscle paralysis
- Arterial oxygen saturation >95% on FiO2 < 80%
- Tidal volume is equal to or greater than 5 ml/kg
- Respiratory rate between 8 and 32
- ETCO2 equal to or less than 55 mmHg

Initial pain control in the ICU, if needed, was with morphine or hydrocodone, given IV every 3-5 minutes until hypertension and tachycardia were controlled as previously mentioned, and/or a pain level of 6/10 was achieved. Following this, all patients were placed on a morphine patient-controlled analgesia pump (1.5 mg bolus; lockout = 6 minutes; maximum = 40 mg/4 hour period) without a loading dose. The total dose of administered morphine in the first 24 hours was recorded. The patients had been asked to grade the intensity of their pain using the visual analog scale (as per SICU protocol), using 0 to indicate no pain, and 10 the most excruciating pain imaginable. The initial recording of this parameter followed arrival in the SICU for the patients extubated in the operating room, or the time of extubation in the SICU, for those not able to be extubated in the OR.

Patients had been evaluated and discharged from the SICU at the discretion of an intensivist. The patients were followed throughout their hospital stay for possible complications associated with spinal injection of opioids (pruritus, respiratory depression, nausea and vomiting and headache). All patients were observed for signs of spinal cord compromise, such as radicular back pain or progressive motor or sensory deficit.

Statistical analysis was performed using Student's t-test for continuous data such as VAS pain, 24-hour morphine utilization, time to extubation and gas exchange data as examined by PaO2/FiO2, bicarbonate ion concentrations, and post-extubation partial pressures of carbon dioxide. Fisher's exact test was performed to compare the number of the patients extubated on the operating table and also to compare the incidence of complications associated with intrathecal administration of opioids. Null hypotheses were rejected for p values less than 0.05.

RESULTS

Demographic data of the 133 patients included in this study revealed no difference in age (61.3 ± 2.5 years vs. 63.1 ± 2.1), ASA status (3-4), preoperative cardiac function (NYHA 2-3) or state of angina (CSS class 3-4) between the IT and IV groups. CABG accounted for 85% of the patients, 7% had valve repair or replacement and the remaining 8% underwent a combined valve and CABG procedure. There was no difference in distribution of the type of surgery between the two groups.

Intraoperative use of fentanyl was lower in the IT group compared to the IV group (1140 ± 210 μg vs. 2050 ± 225 μg; $p<0.05$). The group receiving IT opioids demonstrated quicker time to awakening and less pain at first assessment in the SICU(VAS = 2 vs. 7), or at 24 hours (VAS = 3 vs. 5) (Figure 1, $P<0.05$ for both). The IT group required less morphine as administered by a PCA pump for the 24 hour period immediately following surgery compared to the IV group (11.4 ± 3.1 vs. 52.6 ± 6.2 mg; $P<0.05$) (Figure 2).

{image:1}

{image:2}

{image:3}

Seventy-three percent of the patients (n = 48) in the IT group were extubated in the operating room, compared to 11.5% (n = 8) of patients from the IV group ($p<0.05$). The remaining patients from both groups were generally extubated within 5 hours of their arrival in the SICU. Time-to-extubation of the patients in both groups, brought to the SICU with endotracheal tubes in place, was not significantly different (3.6 ± 2.2 h for 16 patients in the IT group vs. 4.8 ± 1.2 h for 61 patients in the IV group).

Two patients in the IT group, and 5 patients in the IV group required reintubation. In the IT group, 1 patient developed respiratory depression following intravenous bolus of lidocaine (2 mg/kg) that was administered for an episode of ventricular tachycardia, and the other developed apnea following administration of midazolam for restlessness. In the IV group, 3 patients were reintubated because of respiratory depression (following intravenous administration of morphine and/or midazolam for restlessness), and two patients due to hemodynamic instability.

All patients received supplemental oxygen, upon extubation, via a rebreather facemask (FiO2 between 50 - 80%) to maintain oxygen saturation above 92%. Post-extubation

PaCO2 levels were lower in the IT group when compared to the IV group, (45.3 ± 3.7 mmHg vs. 56.1 ± 4.1).

{image:4}

There were no differences between the two groups with respect to SICU stay, duration of hospitalization, and incidence of nausea. After extubation, 5% of patients in that group required treatment (nalorphine) for their pruritus.

DISCUSSION

Including intrathecal opioids in the anesthetic plan led to decreased incidence of required postoperative ventilatory assistance in the IT group, while allowing significantly better pain control that lasted for at least 24 hours. This is associated with a lower requirement of intraoperative as well as postoperative opioids. Whether this is due to better hemodynamic control, more appropriate analgesia, or investigator bias, cannot be discerned from the present data.

The use of intrathecal injection for postoperative pain control in not a new concept. High dose intrathecal morphine (at the range of 1-4 mg) has been used after cardiac surgery with improvement of the quality of pain relief and pulmonary function (11,12). However, the use of high doses of morphine may prolong extubation time. The patients, in those studies, were electively ventilated overnight, postoperatively.

With the advent of interest in reducing variability in anesthesia technique, and in early extubation and “fast-tracking” to reduce the length of ICU stay, “standardization” of our anesthetic protocol for cardiac surgery had been implemented. Among other goals, these modifications had been made to improve postoperative pain management and reduce the risk of postoperative hypoventilation. The intrathecal dose of morphine in the present cases was decided based upon previously published results by Jacobson et al. ([14,15,16]). Addition of shorter acting opioids such as sufentanil, and reducing the morphine dose, has been suggested by other investigators (13).

The present data suggests that patients receiving IT opioids may actually exhibit less ventilatory depression than patients treated solely with IV opioids in the perioperative period. Patients in the IT group were noted to meet extubation criteria more readily at the end of surgery than patients in the IV group. We were able to extubate almost three quarters of patients in the IT group; six times more than in the IV group. The lower partial pressures of CO2 in the IT group also reflects a better preservation of ventilatory derive.

The ability to separate the physiologic effects of analgesia from respiratory depression is certainly an alternative explanation. Although neuraxial morphine and sufentanil have been known to cause respiratory depression, sometimes for protracted periods of time ([17,18]), administered in appropriate doses, it is possible to affect profound pain relief with these agents, without the associated respiratory depression ([19]).

The incidence of respiratory depression was reported to be 1.9% in patients who received 0.03 mg/kg morphine intrathecally for post-surgical pain relief ([20]). Our results were with patients who had received approximately 25% of that dose of morphine, but with a 30 µg supplement of sufentanil. Two patients in our IT group required reintubation; one most likely due to midazolam administration, the other temporally related to lidocaine administration. Our data correlate well with the previously reported incidence of respiratory depression.

Another possible mechanism for our observations is that while IV administration of opioids results in occupation of both spinal and supraspinal receptors, there is a predominance of spinal (kappa) receptors occupied by intrathecal administration of these agents. Respiratory depression has been described following neuraxial administration of opioids, and is thought to be due to cephalad spread via the cerebrospinal fluid ([21]). Respiratory depression is subserved by mu receptors, and there are very few of these below the medulla oblongata in the spinal cord (19). Unless increased dosages and/or longer duration agents are used, respiratory depression should not manifest.

Many anesthesiologists are reluctant to use neuraxial route of administration in patient who will be fully anticoagulated due to fear of possible peridural hematoma formation. The present study, however, is compatible with others that have shown that this is an extremely remote possibility, and that systemic anticoagulation, initiated 1-2 hours after insertion of the spinal needle does not increase the incidence of peridural hematoma ([22,23]). Most of the reported epidural hematomas reported have been in patients undergoing thrombolytic therapy or were anticoagulated at the time of the neuraxial procedure (9, [24,25,26,27,28]). A possible explanation for this is that heparin lacks a thrombolytic effect, and the coagulation process and clot formation is completed by the time of systemic anticoagulation during cardiac surgery ([29,30]). In addition, the smaller guage needle

used for spinal injection is less traumatic when compared to larger size epidural needles ([31,32]).

We conclude that patients in the intrathecal group clearly were more comfortable, and required less postoperative analgesics. These results alone would justify more widespread use of the technique. There is, however, that remote possibility of peridural hematoma, which still has to be cautioned about. The technique does represent an advance in our ability to provide a smooth transition from surgical anesthesia to postoperative awakening with good analgesia, with minimal cognitive and respiratory depression. It is a useful adjunct to our rapid recovery protocols.

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