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Spinal (Subarachnoid) Morphine for Off-Pump Coronary Artery Bypass Surgery

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ABSTRACT

Objective: To study the effects of 8 µg/kg preoperatively administered intrathecal morphine sulfate on extubation time, postoperative pulmonary function, and postoperative analgesia after off-pump coronary artery bypass grafting (OPCAB).

Design: A prospective, randomized, double-blind, placebo-controlled study.

Participants: One hundred adult patients scheduled for elective primary OPCAB.

Interventions: Patients were randomized to preoperative administration of 8 µg/kg intrathecal morphine sulfate (group 1) with a 25-gauge spinal needle or to receive sterile normal saline placebo subcutaneously (group 2). Anesthetic induction and maintenance were standardized to allow planning for facilitating early tracheal extubation. Multivessel OPCAB was performed with an Octopus stabilizer. Patients were extubated in the intensive care unit by a blinded observer using predefined extubation criteria.

Measurements and Main Results: Postoperative times to extubation were 9.47 ± 3.83 hours in group 1 versus 11.25 ± 3.94 hours in group 2 (P = .025). Postextubation bedside spirometric lung volumes in percentage of preoperative lung volume showed significant differences in group 1 versus group 2 in forced vital capacity, 39.66% ± 15.42% versus 31.85% ± 11.65% (P = .016); forced expiratory volume in the first second, 44.8% ± 16.18% versus 35.97% ± 13.32% (P = .013); maximum voluntary ventilation, 39.40% ± 13.57% versus 33.11% ± 14.80% (P = .056); and expiratory flow rate, 47.76% ± 24.61% versus 37.37% ± 4.33% (P = .031). The visual analog pain scores at rest and during coughing at time intervals of 6, 12, 24, and 36 hours postoperatively showed significantly better results in group 1 compared with group 2. The total dose of fentanyl citrate required intraoperatively was significantly less in group 1 (P = .00). One patient in group 1 had a low respiratory rate, which responded to injection naloxone. There was no mortality or neurological complication in either group.

Conclusion: Intrathecal morphine provided superior quality of analgesia that translated into better maintenance of postoperative lung volume determined by spirometry. This analgesic method also facilitated earlier tracheal extubation without any major respiratory or neurologic complications.

INTRODUCTION

Postoperative pain after coronary artery bypass grafting (CABG) is a major cause of respiratory morbidity and can be severe owing to the discomfort of median sternotomy and the effects of spreading the sternotomy to involve intercostal joints, shoulder girdle, rib-vertebral joints, and anterior chest wall muscles. Patients may avoid taking deep breaths, a habit that leads to retention of secretions, atelectasis, and pneumonia. Adequate analgesia is a prerequisite for effective coughing, deep breathing, and weaning from mechanical ventilation.

Use of intrathecal morphine (ITM) in cardiac surgery was first reported by Mathews and Abrams in 40 patients, who had good results [Mathews 1980]. Since then many studies have been conducted to investigate varying doses of ITM, either alone [Fitzpatrick 1988, Vanstrum 1998] or in combination with a short-acting opioid for intraoperative analgesia [Shroff 1994, Zarate 2000, Bettex 2002]. The benefits of spinal analgesia in the care of cardiac surgical patients include improved analgesia and patient comfort, shortened time to extubation [Shroff 1994], improved peak expiratory flow rate, better control of postoperative hypertension [Vanstrum 1998], and possibly a reduction in intensive care unit (ICU) and hospital stay. With the advent of off-pump CABG (OPCAB), there has been a great deal of interest in fast-tracking these patients. Despite the potential advantages of

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neuraxial analgesic techniques, intrathecal opioids have failed to achieve widespread acceptance in cardiac surgery owing to concerns about postoperative respiratory depression and increased risk of neuraxial hematoma formation after administration of heparin during myocardial revascularization. Intrathecal analgesia entails a lower risk of hematoma formation than epidural access [Moen 1996]. Respiratory depression is significant with higher doses of ITM [Fitzpatrick 1988, Jacobson 1988, Taylor 1996]. Recent studies with low-dose ITM have shown effective postoperative analgesia with minimal respiratory depression [Alashemi 2000, Zarate 2000, Bettex 2002].

Our study was designed to examine the effects of low-dose preservative-free ITM, 8 μg/kg administered during anesthetic induction, for fast-tracking these patients and to assess the effects on quality of postoperative analgesia and respiratory function.

MATERIALS AND METHODS

With the approval of the institutional ethics committee and after giving written informed consent, 100 adult patients with well preserved (>40%) left ventricular ejection fraction (EF), and well preserved pulmonary function who were scheduled for elective OPCAB participated in the study. Patients were randomized into 2 groups. Group 1 received 8 μg/kg ITM, and group 2 received placebo sterile normal saline by subcutaneous injection into the back. All injections in both groups were given by a single anesthesiologist not involved with perioperative patient care.

Patients were excluded from the study if they had 1 of the following conditions: significant left main coronary artery disease; unstable angina; EF <40%; associated significant valvular pathology; emergency procedure; reoperation; other major organ dysfunction; preoperative treatment with heparin, warfarin derivatives, aspirin, or clopidogrel within 7 days of surgery; bleeding diathesis; low platelet count (<1,00,000/mm^3); fever; and signs of infection.

The surgeons agreed that the surgery would be delayed for 24 hours if a bloody dural tap occurred.

Ongoing antihypertensive medications were continued until the morning of surgery. All patients received 2 mg oral lorazepam and 150 mg ranitidine the night before surgery and on the morning of surgery. Morphine sulfate, 0.01 mg/kg, was administered intramuscularly 1 hour before the patient was transferred to the operating room.

In the operating room, routine monitoring was instituted with 5-lead electrocardiography, pulse oximetry, direct femoral arterial pressure, and pulmonary artery pressure monitoring with thermodilution cardiac output through the right internal jugular vein. All invasive cannulations for monitoring were done under local anesthesia with 1% lidocaine. Patients were placed in the lateral decubitus position. The skin over L2-3 or L3-4 was infiltrated with 1% lidocaine. Patients in group 1 received 8 μg/kg preservative-free morphine diluted in 2 mL sterile normal saline solution and administered through a 25-gauge Quincke tipped spinal needle after free flow of cerebrospinal fluid was obtained. No more than 3 attempts were allowed in any patient, beyond which the patient was excluded from the study. Subjects in group 2 received a 2 mL sterile normal saline solution by subcutaneous injection over the back. An adhesive band was applied to the back for maintaining blinding of the patient and perioperative investigators.

Anesthesia was induced with 4 μg/kg fentanyl citrate, 0.04 mg/kg midazolam, and 1.5 to 2.0 mg/kg propofol. Endotracheal intubation was facilitated with 0.08 mg/kg vecuronium bromide. Anesthesia was maintained with a continuous infusion of propofol at 4 to 6 mg/kg per hour, intermittent administration of fentanyl citrate at 3 μg/kg per hour, 0.04 mg/kg vecuronium bromide, and 0.02 to 0.03 mg/kg midazolam. To achieve an activated clotting time of 250 to 300 seconds only 90 minutes after the spinal injection in all patients, 2 mg/kg heparin was administered before myocardial revascularization was begun. Myocardial revascularization was achieved in all patients without the use of cardiopulmonary bypass (CPB) with the aid of a myocardial stabilizer (Octopus III; Medtronic, Minneapolis, MN, USA). Heparin was neutralized with protamine at the completion of revascularization. Normothermia was attempted in all patients intraoperatively with the aid of forced air warmers, warmed intravenous fluids, and a circulating warm water mattress beneath the patient.

On completion of the surgery, all patients were transferred to the postoperative ICU, where an observer blinded to patient group made all observations. Postoperative care was standardized, and early tracheal extubation was planned for all patients. All patients received elective ventilation for 2 to 3 hours postoperatively and were sedated with propofol infusion, 1.5 to 2 mg/kg per hour. They were then assessed and weaned from the ventilator through synchronized intermittent mandatory ventilation and pressure support ventilation. Criteria for extubation included adequate neurological recovery, stable arterial blood gases on inspired oxygen concentration <0.5, minimal chest tube drainage, hemodynamic stability, normothermia, and satisfactory urine output (>1 mL/kg per hour). Total doses of fentanyl citrate and vecuronium bromide administered intraoperatively were obtained from the anesthesia notes. A visual analog scale (VAS) of 10 cm was used for assessment of pain at rest and on coughing, 0 being no pain and 10 being maximum pain. All patients received intravenous tramadol, 1.5 mg/kg every 8 hours. Analgesia was supplemented with intravenous morphine (2-5 mg) in patients receiving ventilation or intramuscular diclofenac sodium (1.5 mg/kg) in extubated patients who complained of increased intensity of pain (VAS >4). Bedside spirometry was performed for all patients 2 hours after removal of chest tubes in the ICU. Time for awakening (eye opening to oral command) and tracheal extubation were noted.

Patient hemodynamic and oxygenation parameters were recorded at specific events, as follows: 5 minutes after anesthetic induction (before skin incision) (event 1), 10 minutes after sternotomy (event 2), 15 minutes after myocardial revascularization (event 3), before extubation (event 4), and 1 hour after extubation (event 5).

The following blood samples were collected for analysis of inflammatory markers: superoxide dismutase (SOD), glutathione peroxidase (GPEROX), interleukin 6 (IL-6), and

Table 1. Patient Characteristics*

	Group 1 (n = 53)	Group 2 (n = 47)	*P*
Age, y	58 ± 9	58 ± 9	NS
Male, n	48	45	NS
Female, n	5	2	NS
Height, cm	165 ± 8	164 ± 7	NS
Weight, kg	71 ± 11	70 ± 9	NS
Hypertension, n	31	31	NS
Diabetes mellitus, n	29	30	NS
Pulmonary function tests			
FVC, %	88 ± 18	92 ± 15	NS
FEV_1, %	91 ± 20	97 ± 16	NS
FEV_1/FVC	105 ± 9	107 ± 6	NS
MVV, %	78 ± 24	86 ± 19	NS
PEFR, %	85 ± 23	93 ± 23	NS

*All results are expressed as mean ± SD or number of patients. NS indicates not significant; FVC, forced vital capacity; FEV_1, forced expiratory volume in the first second; MVV, maximal voluntary ventilation; PEFR, peak expiratory flow rate.

tumor necrosis factor α (TNFα) in addition to total leukocyte count (TLC) and differential leukocyte count (DC) at the following time intervals: 5 minutes after anesthetic induction (A), 10 minutes after sternotomy (B), 15 minutes after myocardial revascularization (C), and postoperatively at 2, 12, and 24 hours (D, E, F).

Postoperative complications were recorded daily until the patients were discharged from the ICU. After extubation, patients were directly questioned about the occurrence of pruritus, nausea, and vomiting. A rise of postoperative creatinine kinase myocardial band fraction >10% of the total creatinine kinase or appearance of new Q waves on an electrocardiogram was considered to be significant for the diagnosis of postoperative myocardial infarction.

Statistical Analysis

Pearson chi-square or Fisher exact test, whichever is applicable, was used for comparison of categorical variables between the 2 groups. Student *t* test was used to test the difference of means between the 2 groups. Values are presented as mean ± SD. Independent-samples *t* test was used to test the difference of means between the 2 groups. A *P* value <.05 was considered statistically significant.

For analyzing inflammatory markers and oxygenation parameters (alveolar-arterial oxygen difference [$P_{AO_2} - Pa_{O_2}$] and pulmonary shunt fraction [Qs/Qt]), multiple analysis of variance for repeated measures was carried out for comparison between different stages and groups.

RESULTS

Of the 100 patients enrolled in our study, 53 were randomized to group 1 and 47 to group 2. The 2 groups had similar demographic characteristics (Table 1).

The time to heparinization was more than 90 minutes from the intrathecal injection in all patients. No bloody tap occurred in any patient. Intraoperative data are shown in Table 2. No patient needed intraaortic balloon counterpulsation or institution of CPB during the surgical procedure. Postoperative observations are given in Table 3. Nineteen patients were extubated within 6 hours of arrival in the ICU. Group 1 patients had earlier awakening than those in group 2 (133 ± 86 minutes versus 170 ± 82 minutes, *P* = .033). Twenty-seven patients were ventilated for more than 12 hours in the ICU for different reasons, including hemodynamic instability, low arterial oxygenation, and significant chest tube drainage. There was no significant difference between the 2 groups postoperatively in incidence of postoperative ST-T segment changes. No patient in either group had perioperative myocardial infarction.

Table 2. Intraoperative Data*

	Group 1	Group 2	*P*
Surgical time, min	226 ± 47	236 ± 50	NS
No. of grafts	2.2 ± 0.8	2.7 ± 0.8	NS
Fentanyl dose, μg	432 ± 125	625 ± 235	NS
Vecuronium dose, mg	16 ± 5.1	17 ± 5.2	
Sweating, n	3	2	NS
Epinephrine infusion, n	4	5	NS
Norepinephrine infusion, n	6	6	NS

*All results are expressed as mean ± SD or number of patients. NS indicates not significant.

Patients in group 1 had significantly better VAS scores both at rest and while coughing compared with patients in group 2. Thirteen patients had postextubation pulmonary complications of atelectasis, consolidation, or mild hypoxemia necessitating a higher concentration of oxygen therapy. The incidence was similar in the 2 groups. Two patients in group 1 reported pruritus, which responded to diphenhy-

Table 3. Postoperative Data*

	Group 1	Group 2	*P*
Time awake, min	133 ± 86	170 ± 82	.033†
Time extubated, h	9.5 ± 3.9	11.2 ± 3.9	.028†
Forced vital capacity, %	39.7 ± 15.4	31.9 ± 11.7	.016†
Forced expiratory volume in the first second, %	44.8 ± 16.2	36.0 ± 13.3	.013†
Maximal voluntary ventilation, %	39.4 ± 13.6	33.1 ± 14.8	.056
Peak expiratory flow rate, %	47.8 ± 24.6	37.4 ± 14.3	.03†
VAS rest 12 h	3.4 ± 3.4	4.8 ± 2.7	.00†
VAS cough 12 h	3.8 ± 3.4	6.06 ± 2.0	.00†
VAS rest 24 h	2.03 ± 1.5	4.0 ± 1.9	.00†
VAS cough 24 h	3.09 ± 1.5	5.7 ± 1.1	.00†
VAS rest 36 h	2.58 ± 1.3	4.3 ± 1.9	.00†
VAS cough 36 h	3.5 ± 1.2	5.7 ± 1.0	.00†
Postextubation $Paco_2$, mm Hg	43.1 ± 5.1	40.4 ± 3.0	.011†

*All results are expressed as mean ± SD or number of patients. VAS indicates visual analog pain score; $Paco_2$, arterial carbon dioxide tension.

†Statistically significant.

Table 4. Postoperative Analgesia

	Group 1	Group 2	*P*
Intravenous morphine	8/53 (15.1%)	15/47 (31.9%)	
Intravenous diclofenac sodium	11/53 (20.8%)	7/47 (14.9%)	.145
No analgesic supplement needed	34/53 (64.2%)	24/47 (51.1%)	.089

dramine. One patient in group 1 developed postextubation respiratory depression (respiratory rate, <8/min; $PaCO_2$, 61 mm Hg), which was treated with 0.4 mg intravenous naloxone but did not necessitate reintubation. There were no neurologic complications in either group. Postoperative spirometric volumes were better preserved in group 1 than group 2 (Table 3). Time to mobilization, stay in the ICU, and hospital stay were similar in the 2 groups. Sixteen patients in group 1 and 26 in group 2 needed rescue analgesics for breakthrough pain; however, the difference did not reach statistical significance (Table 4).

The results of analysis of biochemical oxygenation parameters ($PA_{O_2} - Pa_{O_2}$ and Qs/Qt) are shown in Tables 5 and 6. Both parameters increased intraoperatively and gradually normalized postoperatively. The variation was significant within each group; however, intergroup variation was not statistically significant.

There have been numerous reports in the literature on inflammatory markers in cardiac surgery performed with CPB; however, there have been few reports of OPCAB with ITM. SOD, GPEROX, TNFα, IL-6, and TLC were serially analyzed at different predetermined time intervals in all patients. The variations in TLC and SOD were significant compared with baseline values in each group. Intergroup variation was not significant for the inflammatory markers analyzed in the study.

DISCUSSION

Mathews and Abrams (1980) first reported the use of 1.5 to 4.0 mg ITM in 40 patients undergoing open heart surgery. Seventeen of the patients did not need any analgesic treatment in the entire postoperative course. ITM is an effective, convenient, and simple technique for management of postoperative pain. A single dose often suffices as the sole analgesic for the entire postoperative period, effects persisting for 30 to 36 hours postoperatively [Wang 1979, Mathews 1980]. The neuraxial technique of analgesia with opioids and local anesthetics has several benefits, such as improved analgesia, attenuation of the stress response, thoracic cardiac sympathectomy [Chaney 1997b], attenuation of a rise in troponin level [Chaney 1997a], and antiischemic effects [Loick 1999]. Intrathecal opioid analgesia provides intense analgesia without motor blockade and maintains sympathetic tone, thereby avoiding hypotension.

In most reports of ITM used alone or in combination with a short-acting opioid, the aim was prolonged postoperative analgesia. Intense analgesia with continuous intravenous fentanyl or sufentanil infusion in neonatal cardiac surgical patients was associated with decreases in blood epinephrine and norepinephrine levels and decreased morbidity and mortality [Anand 1992]. Early postoperative myocardial ischemia may be associated with adverse cardiac outcome and can be reduced by intense analgesia [Mangano 1992].

Varying doses of ITM have been used in different studies, but the optimal dose for adequate postoperative analgesia without respiratory depression is uncertain [Mathews 1980, Fitzpatrick 1988, Taylor 1996, Alashemi 2000, Bettex 2002]. The time for onset of action of ITM is approximately 15 to 45 minutes [Wang 1979] with a duration of action of 24 to 36 hours [Yaksh 1981]. In more recent studies investigators have used lower doses of ITM (5-8 μg/kg) and reported excellent analgesia with minimal respiratory depression [Nader 2000, Zarate 2000, Bettex 2002]. We used a dose of 8 μg/kg ITM in our study group of patients. Because of its lower lipid solubility and slow onset of action, such a low dose of ITM is unlikely to initiate reliable intraoperative analgesia [Vanstrum 1998]. Chaney et al [1996] did not find any attenuation of stress response during or after CABG after preoperative large-dose ITM (4 mg). However, the postoperative stress response may be attenuated by intense analgesia. ITM in a dose of 0.5 mg was shown to reduce analgesic and antihypertensive requirements after CABG [Vanstrum 1998]. Recent studies of ITM for CABG have been focused on earlier tracheal extubation and fast-tracking these patients, and the results have varied [Chaney 1997b]. Our anesthetic technique was aimed at fast-tracking OPCAB patients. The decreased need for intraoperative use of fentanyl citrate in group 1 suggested an analgesic response of ITM in the intraoperative period. The result was earlier postoperative awakening (133 ± 86 minutes in group 1 versus 170 ± 82 minutes in group 2) and relatively early tracheal extubation (9.5 ± 3.9 hours in group 1 versus 11.3 ± 3.9 hours in group 2). Postoperative analgesia was excellent in our study group as evidenced by significantly lower VAS scores, which translated into better preservation of lung volumes at bedside spirometry (Table 3). There was no significant difference between the 2 groups with respect to need for parenteral opioid/nonopioid analgesics.

Table 5. Oxygenation Parameters*

	$PA_{O_2} - Pa_{O_2}$ (1)	$PA_{O_2} - Pa_{O_2}$ (2)	$PA_{O_2} - Pa_{O_2}$ (3)	$PA_{O_2} - Pa_{O_2}$ (4)	$PA_{O_2} - Pa_{O_2}$ (5)	*P*
Group 1	173.4 ± 66.3	194.2 ± 90.1	230.6 ± 109.6	153.6 ± 48.9	105.2 ± 48.1	.00†
Group 2	138.4 ± 76.0	158.3 ± 49.4	199.2 ± 87.1	138.2 ± 43.6	96.3 ± 36.5	.00†

*All values are mean ± SD. $PA_{O_2} - Pa_{O_2}$ indicates alveolar-arterial oxygen tension difference.

†Statistically significant.

Table 6. Pulmonary Shunt Fraction*

	Qs/Qt (1)	Qs/Qt (2)	Qs/Qt (3)	Qs/Qt (4)	Qs/Qt (5)	*P*
Group 1	14.6 ± 6.5	15.9 ± 6.7	19.0 ± 7.0	11.3 ± 3.4	8.6 ± 3.5	.00
Group 2	12.4 ± 5.4	12.9 ± 4.4	16.2 ± 6.6	9.7 ± 3.3	7.7 ± 3.3	.00

*All values are mean ± SD. *P* value within either group and between groups 1 and 2. Qs/Qt indicates pulmonary shunt fraction.

The systemic inflammatory response may be initiated during cardiac surgery owing to blood contact with the foreign surface of the CPB apparatus, ischemia-reperfusion injury, and endotoxemia [Hall 1997]. The occurrence of a systemic inflammatory response by the body to various stimuli during CPB is well established. Whether a similar but low-grade response occurs during OPCAB is not clear. IL and TNF are among the few mediators involved in maintenance of systemic inflammation after its initiation.

TNFα is one of the earliest and most important of the endogenous mediators released in the inflammatory response following activation of macrophages and other proinflammatory cells [Giroir 1993]. Endotoxin is a potent stimulus for TNF production. TNF leads to hypotension, fever, increased production of acute-phase reactants, and reduced serum albumin level [Hall 1997]. The unlikely presence of a stimulus for TNF production explains the lack of significant variability among the 2 groups in the study.

IL-6 levels have been shown to increase during CPB [Cremer 1996]. No significant variation was found in IL-6 levels in the 2 groups in our study.

SOD is an antiinflammatory antioxidant enzyme produced by the body for scavenging oxygen free radicals released in response to inflammation and ischemia and reperfusion. Low SOD levels imply free radical release. Although the variation in SOD levels in either group was significant, suggesting increasing oxygen free radical release in the first 24 hours perioperatively, no significant association between the 2 groups was established.

Local anesthetics appear to have greater efficacy than opioids in attenuation of the stress response, probably because of their unique mechanism of action. ITM, owing to its intense analgesia, may attenuate the stress response postoperatively [Vanstrum 1998]. This phenomenon suggests the possibility that ITM has a role in blunting the systemic inflammatory response in cardiac surgery. As shown in Tables 5, 6, and 7, ITM did not have significant comparable effects on oxygenation parameters and inflammatory markers in the 2 groups studied.

ITM is associated with 4 major side effects—ventilatory depression, pruritus, nausea and vomiting, and urinary retention. Ventilatory depression with ITM is dose dependent, potentiated by intravenous sedatives and opioids, advanced age, coexisting diseases, increased intrathoracic pressure, and patient position [Chaney 1995]. The incidence of respiratory depression with high-dose ITM (0.03 mg/kg) in cardiac surgical patients is 1.9% [Taylor 1996]. Patients in group 1 had slightly higher values of arterial carbon dioxide tension, and only 1 patient developed significant respiratory depression, which necessitated only naloxone therapy. The incidence of nausea and vomiting was similar in the 2 groups.

Good postoperative analgesia and lung function enabled our study group patients to be weaned earlier from ventilatory support with minimal side effects.

Intrathecal injection in cardiac surgical patients needing intraoperative therapeutic anticoagulation entails the serious risk of epidural hematoma formation and subsequent neurologic injury. The estimated incidence of hematoma formation is approximately 1:220,000 [Vandermeulen 1994] after intrathecal injection. Intrathecal injection has a lower risk of hematoma formation than epidural instrumentation because of the smaller size of needles used and the prominence of the venous plexus in the epidural space. Continuous catheter techniques carry higher risk than single injection because

Table 7. Inflammatory Response*

Variable	Group	Event A	Event B	Event C	Event D	Event E	Event F
TLC	1	6651 ± 1508	7577 ± 1642	13,132 ± 5456	17,291 ± 5720	13,973 ± 4196	13,297 ± 3825
	2	6609 ± 1375	7206 ± 1757	13,063 ± 5694	16,160 ± 5121	14,936 ± 4551	14,415 ± 4288
SOD	1	59.7 ± 32.4	61.9 ± 41	55.06 ± 34.5	51.5 ± 32.0	42.8 ± 29.3	45.4 ± 30.1
	2	67.3 ± 43.5	60.0 ± 43.1	51.0 ± 31.5	49.1 ± 32.0	42.1 ± 23.5	44.8 ± 29.2
GPEROX	1	4256 ± 2486	4424 ± 3745	4359 ± 2878	4175 ± 2049	4394 ± 2413	4395 ± 2502
	2	5132 ± 3419	5098 ± 3253	4780 ± 3288	3613 ± 2155	4184 ± 3145	4810 ± 3160
IL 6	1	199.6 ± 212.2	174.7 ± 215.2	183.3 ± 276.9	149.3 ± 182.9	142.2 ± 178	195.7 ± 306.9
	2	248.5 ± 293.0	242.2 ± 272.5	284.4 ± 355	219 ± 225	212.5 ± 239.9	192.5 ± 204
TNFα	1	2.02 ± 2.68	1.85 ± 1.03	1.69 ± 1.47	1.78 ± 1.11	1.72 ± 0.94	2.93 ± 5.50
	2	2.97 ± 7.06	1.67 ± 0.87	2.14 ± 2.89	1.79 ± 0.87	2.12 ± 1.30	2.80 ± 5.73

*All values are mean ± SD. TLC indicates total leucocyte count in percentage mm of blood; SOD, superoxide dismutase; GPEROX, glutathione penoxidase; IL 6, interleukin 6; TNFα, tumor necrosis factor α.

hematoma formation can occur during catheter removal. No case of epidural hematoma has been reported after ITM in cardiac surgical patients [Rao 1981, Vandermeulen 1994]. However, the safety of such a technique is controversial, and the risk may be as high as 0.035% [Owens 1986]. Certain precautions may decrease this risk [Rao 1981, Vandermeulen 1994]. Proper selection of patients, an atraumatic spinal injection technique, a readiness to postpone surgery with strict neurologic monitoring for 24 hours in the event of a bloody tap, allowing a minimal interval of 60 to 120 minutes between spinal injection and heparinization, close monitoring of activated clotting times, and intraoperative heparin reversal all are important recommendations for avoiding spinal hemorrhagic complications and improving the safety of this technique. Our exclusion criteria with respect to this complication were specifically strict, and the surgeons agreed to delay surgery in case of a bloody tap.

Our patients were not fully heparinized because all procedures were OPCAB, in which patients are supposed to be hypercoagulable postoperatively.

CONCLUSION

ITM at a dose of 8 μg/kg for OPCAB is effective for excellent postoperative analgesia, preserves lung volumes with minimal undesirable effects, and facilitates early tracheal extubation. Judicious incorporation of intrathecal analgesic techniques for OPCAB would enhance fast-tracking and improve patient comfort with the potential for reducing ICU stay and hospital costs.

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