Journal of Anesthesia & Clinical Research

Dabbagh et al. J Anesthe Clinic Res 2011, 2:5
DOI: 10.4172/2155-6148.1000139

Research Article Open Access

The Effect of Intrathecal Bupivacaine Plus Sufentanil on Intraoperative Hemodynamics During Elective Coronary Artery Bypass Surgery

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Abstract

Introduction: Intrathecal opioids have been used for many patients undergoing surgical operations to improve clinical outcomes. Cardiopulmonary bypass in patients undergoing coronary artery bypass graft surgery carries a number of drawbacks, namely hemodynamic derangements. Several methods have been used to suppress this state; among them is sympathetic blockade by neuraxial anesthesia. This study assesses the effect of intrathecal adjuvant bupivacaine plus sufentanil on intraoperative hemodynamic changes in elective coronary artery bypass surgery.

Methods: In a double-blind, randomized, placebo-controlled clinical trials, 80 patients scheduled for elective CABG were randomly assigned into 2 groups. One group received intrathecal sufentanil (S) and the other group received the same dose of sufentanil plus supplemental bupivacaine (SB). All the patients were similar regarding other items. Hemodynamic and clinical outcomes including blood pressure values were measured during and after the operation.

Results: There were more stable hemodynamic parameters in the SB group. Also, the SB group patients were extubated sooner than the other patient group.

Discussion: The administration of intrathecal sufentanil plus bupivacaine seems to keep the hemodynamic status of the patients more stable than intrathecal sufentanil alone.

Keywords: Cardiopulmonary bypass; Coronary artery bypass surgery; Mean arterial pressure

Introduction

Intraoperative hemodynamic stability is always a major concern for anesthesiologist and the surgeon caring for the patients, especially those undergoing coronary artery bypass graft surgery.

Intrathecal opioids have been used for many patients undergoing surgical operations to improve clinical outcomes [1,2]. Also, patients undergoing coronary artery bypass graft surgery using cardiopulmonary bypass (CPB) would tolerate a number of drawbacks, including hemodynamic derangements [3-5]. Several methods have been used to blunt these hemodynamic alterations which maybe accompanied with aggravated inflammatory state usually seen in patients undergoing CPB; sympathetic blockade by neuraxial anesthesia may be mentioned as one of these methods, including high-dose intrathecal bupivacaine combined with general anesthesia [5,6].

This study assesses the effect of intrathecal bupivacaine plus sufentanil on intraoperative hemodynamic changes in elective coronary artery bypass surgery.

Materials and Methods

The protocol of the study was approved by the institutional Ethics Committee for meeting the ethical considerations. In a double-blind, randomized clinical trial, the target population was considered as all the patients who were admitted in the cardiac surgery operating room of a university hospital during a 12-month period. Among these cases, the total number of study sample size was calculated: 80 consecutive patients randomly divided into 2 groups (40 cases in each group) according to a computer table of random numbers; all had a visit the night before their operation by one of the colleagues who was an anesthesiologist who obtained informed consent, and information regarding the study was given to them.

Inclusion criteria were elective CABG cases with informed written consent aged 30-75 years and a weight range of 50 to 100 Kg. Those cases who refused to enter the study, had a history of diabetes mellitus, had any underlying coagulation system disease (esp. those with any co-existing bleeding disorders or a history of platelet dysfunction or low platelet number), or had any sign or history denoting past or present spinal diseases, especially those who needed surgeries for it were excluded from the study.

After matching the inclusion and exclusion criteria, induction of general anesthesia was done, then one group received intrathecal sufentanil (S) and the other group received the same dose of sufentanil plus supplemental bupivacaine (SB). Except for this, all the cases were similar regarding anesthesia and surgery. Arterial blood pressures were measured before and after induction of anesthesia, during the bypass time and after weaning from bypass were checked.

One of our colleagues anesthetized the cases inside the operating

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Received December 18, 2010; **Accepted** May 02, 2011; **Published** May 05, 2011

Citation: Dabbagh A, Rajaei S, Taghizade H (2011) The Effect of Intrathecal Bupivacaine Plus Sufentanil on Intraoperative Hemodynamics During Elective Coronary Artery Bypass Surgery. J Anesthe Clinic Res 2:139. doi:10.4172/2155-6148.1000139

room and the other one was present in the room all over the course of the study; only when the first one wanted to administer intrathecal drug(s), the 2nd colleague left the operation room, then came back inside and registered the other data. Because this study was to be double blinded, the anesthesiologist administering the intrathecal drugs was not involved in the management of the patient after intrathecal injection. The first colleague coded each patient according to the allocation table created in advance based on the computer table of random numbers and saved them in a secret manner. The 2nd colleague registered the data regarding the values for blood pressure.

In the study all the patients had a high spinal, then the patients invariably had bradycardia; which would be difficult for the 2nd colleague to detect which group the patient belonged to.

All the patients entered the operating room after having a before-operation night visit and a pre-medication dose of morphine (0.1 mg/kg intramuscular) 1 hour before the surgery. All the patients went on an 8 hour period of Non Per Oss (NPO) for 8 hours before coming to the operation room.

Anesthesia started with the standard monitoring, including electrocardiography, pulse oxymetry, invasive blood pressure, and heart rate; then the patients received 500 ml Ringer's solution over 10–15 minutes. Induction of general anesthesia was done using 0.5μ/Kg intravenous sufentanil plus 1mg/Kg propofol and 100μg/Kg pancuronium. Then the patient was intubated and a central venous line was inserted through the right internal jugular vein.

After induction of anesthesia, the patients were turned to the lateral decubitus position while their head and neck and the other parts of the body were protected. Then, through a sterile paramedian approach, using a No. 25 Whitacre spinal needle, after appearance of the cerebrospinal fluid in the needle hub, intrathecal drug was administered.

The patients in the S group received pure preservative free intrathecal sufentanil in a dose of 0.5μg/Kg; which was equal to 1 ml of the drug per 10 Kg of body weight. The patients in the SB group received the same dose of sufentanil plus supplemental preservative free intrathecal hyperbaric bupivacaine in a dose of 0.5mg/Kg of body weight. Then the patients were turned back to the supine position while protected. Their feet were elevated and the body was head down as much as 20 degrees to make sure upward direction of the intrathecal drug.

The study patients had continuous blood pressure and central venous pressure monitoring all during anesthesia and surgery; these parameters were recorded every five minutes; it means that the blood pressure values were written down in the study checklist every 5 minutes after administration of intrathecal drug, including during the sternotomy, just before starting the cardiopulmonary bypass, during the cardiopulmonary bypass and also during the weaning period from bypass. Also, the vasopressor and fluid requirements were measured and documented for each patient.

A combination of 0.01μg/Kg/min sufentanil plus 0.5mg/Kg/min atracurium and 0.2μg/Kg/min midazolam were used for anesthesia maintenance as intravenous infusion. Also, 0.4 to 0.6% isoflurane was administered by inhalational route. The patients were operated on and were under mechanical ventilation with endotracheal tube, transferred to the post operative cardiac intensive care; until based on the standard criteria for weaning, were weaned and extubated. During the operation, time of operation from the incision to the skin closure, aortic clamp time and the pump time were all registered in patient checklists. Also, the time from patient entry to ICU up to tracheal extubation was registered for each case.

During the course of the study, the patients' personal data were kept confidential, also, the allocation of the patients to the groups was not revealed; also, the patients could decide not to continue the course of the study just by informing one of the colleagues. For data entry and analysis SPSS software (version 11.5) was used. Also, Student t test and Chi square test were used for analysis of the final data. Mean ± SD was used for demonstrating the results; a P value less than 0.05 was considered significant.

Results

The two groups had no statistically significant difference regarding age, sex, body weight, duration of surgery, aortic cross clamp time and extracorporeal Circulation time (Tables 1 and 2).

There were as a number of significant differences in mean, systolic and diastolic arterial pressure values between the 2 groups which are demonstrated in Table 3. The differences between the mean, diastolic and systolic pressures before and during sternotomy and during the cardiopulmonary bypass are to be mentioned; which shows fewer increases in blood pressure after incision and during sternotomy. Also fewer drops in blood pressure were seen after start of the bypass. There was no statistically significant difference after weaning from cardiopulmonary bypass and also, regarding the time for extubation between the two groups.

The two groups had no statistically significant difference regarding neither the needed vasopressor dose nor the fluid requirements during the operation and also, the first postoperative hours.

There was no difference between the two groups regarding the incidence of postoperative hemodynamic, renal, and pulmonary complications. Also, there was not any sign or symptom related to any possible neurologic complication after administration of high dose heparin when the patients were transferred to the intensive care unit. Also, none of the patients complained of post dural puncture headache.

Discussion

The results of this study demonstrated that adding bupivacaine to intrathecal sufentanil could make the blood pressure profile more stable than the same dose of sufentanil in patients undergoing elective coronary artery bypass grafting general anesthesia combined with spinal anesthesia. This method was especially effective after incision, during sternotomy and also, during the cardiopulmonary bypass.

There were a number of limitations to be mentioned in this study: there was no measurement of cardiac output. Also, due to the method of the study, it was not possible to check the sensory blockade of the intrathecal drugs using pinprick test while the patients were awake. If the first try of needle failed, there were no more attempts due to the possibility of any neurologic problem after administration of high dose heparin, so these cases were taken out of the study and may be a limitation of the study. Also, if there was a comparison between the groups regarding the intraoperative transesophageal findings, there may be some other findings noted; this could be mentioned as another limitation of the study.

The use of CPB is associated with the development of an important state known as systemic inflammatory response syndrome (SIRS); this syndrome may affect the outcome of the patients. There are multiple pathways that are linked to the start and continuation of the SIRS It

	S	SB	P value (for t-test)
Age (years)	58 (11)	54 (12)	0.11
Body weight (Kg)	84 (10)	80 (11)	0.12
Duration of the surgery (minutes)	210 (21)	203 (23)	0.19
The time of aortic cross clamp (minutes)	63 (6)	66 (7)	0.09
Extracorporeal Circulation time (min)	91 (9)	87 (12)	0.08

*Data are presented as mean ± (standard deviation)

Table 1: Demographics of the patients in the two groups*.

	S	SB
Male	26	23
Female	14	17

*Chi-square test, degree of freedom = 1, P= 0.32

Table2: Distribution of sex in the two .groups

	SB	S	P value (for t-test)
Before sternotomy**			
MAP***	74±6	82±13	0.00
SAP§	105±7	110±6	0.01
DAP¥	63±7	67±3	0.01
During sternotomy			
MAP	73±9	92±16	0.00
SAP	110±4	142±7	0.00
DAP	55±3	78±4	0.00
After start of CPB ψ			
MAP	65±3	55±4	0.00
SAP	68±6	58±4	0.00
DAP	64±6	53±3	0.00
After weaning from CPB			
MAP	89±13	85±10	0.09 Ψ
SAP	115±10	119±12	0.08 Ψ
DAP	76±4	74±6	0.08 Ψ
Time to extubation Ω	264±68	322±72	0.02

. Data are presented as mean ± (standard deviation)
. Before sternotomy; while the surgical procedure has started
. Mean arterial pressure
§ Systolic Arterial Pressure
¥ Diastolic Arterial Pressure
ψ CPB: Cardiopulmonary Bypass
Ω Calculated from the time of arrival to ICU up to the time of extubation in minutes
Ψ The difference is not statistically significant

Table 3: Demographics of the patients in the two groups*

has been proposed in animal models that this "enhanced inflammatory response with subsequent hypotension may have contributed to mortality" [4].

Although in a previous meta-analysis, it has been concluded that perioperative mortality and morbidity has not been affected in cardiac surgery patients by using spinal anesthesia, this meta-analysis has reviewed only those studies using spinal anesthesia with morphine and one of the 25 studies used in that meta-analysis has used bupivacaine; also, the authors of that study have mentioned that altered drugs and techniques could change the "outlook of comparison" between the standard anesthesia plan and the spinal anesthesia for these cases [7].

In previous studies it has been shown that cardiopulmonary bypass (CPB) plays a major role in the perioperative stress response after following cardiac surgery which is superimposed on the stress response induced by the surgical process and also, the imbalance in pro- and anti-inflammatory responses may affect outcome in cardiac surgery patients [6]. Splanchnic hypoperfusion before the start of CPB and also, during CPB, direct exposure of blood with the surface of the CPB circuit and other factors [6] can increase the severity of the stress response and are all in favor of adverse outcomes in the perioperative period in patients undergoing cardiac surgery with CPB. There are a number of studies that have examined methods to decrease this stress and inflammatory response to make the clinical outcome better.

In one study in patients undergoing coronary artery bypass grafting using thoracic epidural anesthesia combined with general anesthesia attenuated myocardial sympathetic response to cardiopulmonary bypass and cardiac surgery was demonstrated and an association of this finding with decreased myocardial ischemia determined by less release of troponin T was shown [8]. Also, in another study, it was demonstrated that high-dose intrathecal bupivacaine, when combined with general anesthesia, resulted in less β receptor dysfunction and a lower stress response during coronary artery bypass graft surgery [5]. In another study performed in pediatric acyanotic congenital heart disease patients undergoing cardiac surgery under CPB, it has been shown that administration of caudal epidural bupivacaine and sufentanil ends in attenuation of the stress response [9]. All these studies have been focused on the stress response; though there are similarities between these and our study, none have been considering a comparison between intrathecal sufentanil and bupivacaine with sufentanil alone in adult CABG regarding blood pressure changes.

In non-cardiac surgeries, it has been demonstrated that small-dose bupivacaine-sufentanil prevents cardiac output modifications after spinal anesthesia [10]. The measurement of cardiac output was not done in the present study; but maybe in future studies, it could be an appropriate complementary study.

Our study shows that intrathecal bupivacaine and sufentanil can exert a better control of blood pressure before and during the CPB; a finding that shows better control of a major determinants of stress response [5-6] by combination of bupivacaine and sufentanil. So, it seems that this combination could make the clinical course less "stressful" before the CPB " before the CPB with less increase in blood pressure during surgical stimulus and also, preventing less severe hypoperfusion after the start of CPB; a phenomenon contributing to more stress response [6].

Although there is some major concerns regarding possible epidural hematoma after neuraxial block in patients receiving anticoagulants and there are a number of guidelines in this field clearly stating the issue [11], there may be even some other cases having the complication even after coping with the guideline [12].

In one study it was demonstrated that in low-risk patients undergoing CABG or valve surgery, combined intrathecal sufentanil and morphine and an infusion of propofol can have acceptable goals regarding the duration of intubation [13]. The findings of this study also demonstrated similar times for extubation in the two groups receiving intrathecal sufentanil with or without bupivacaine; maybe the administered bupivacaine has decreased the need for intravenous anesthetic drugs, so, time for extubation has been similar in the 2 groups.

Finally, this study suggests that combined general anesthesia and spinally administered sufentanil and bupivacaine yields to a better control of blood pressure during sternotomy and also, before starting and during the course of CPB in adult patients undergoing CABG.

Acknowledgments

The authors would like to acknowledge the ICU and OR nurses and physicians of Cardiac Surgery and Cardiac Intensive Care Wards, Modarres Hospital, Shahid Beheshti University of Medical Sciences for their intraoperative and postoperative

cooperation and caring for the patients during the course of the study.

Conflict of Interest

The authors have no conflict of interest on any drugs or products of the study.

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