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## SCIENTIFIC ARTICLE

# Intrathecal sufentanil for coronary artery bypass grafting

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### KEYWORDS

Cardiac surgery;  
Spinal anesthesia;  
Sufentanil;  
Interleukin 6

### Abstract

**Context:** Cardiac surgery patients undergoing coronary artery bypass grafting with cardiopulmonary bypass.

**Objective:** Evaluate the effect of adding intrathecal sufentanil to general anesthesia on hemodynamics.

**Design:** Prospective, randomized, not blinded study, after approval by local ethics in Research Committee.

**Setting:** Monocentric study performed at Dante Pazzanese Institute of Cardiology, Sao Paulo, Brazil.

**Patients:** 40 consenting patients undergoing elective coronary artery bypass, both genders.

**Exclusion criteria:** Chronic kidney disease; emergency procedures; reoperations; contraindication to spinal block; left ventricular ejection fraction less than 40%; body mass index above 32 kg/m<sup>2</sup> and use of nitroglycerin.

**Interventions:** Patients were randomly assigned to receive intrathecal sufentanil 1 µg/kg or not. Anesthesia induced and maintained with sevoflurane and continuous infusion of remifentanil.

**Main outcome measures:** Hemodynamic variables, blood levels of cardiac troponin I, B-type natriuretic peptide, interleukin-6 and tumor necrosis factor alpha during and after surgery.

**Results:** Patients in sufentanil group required less inotropic support with dopamine when compared to control group (9.5% vs 58%,  $p=0.001$ ) and less increases in remifentanil doses (62% vs 100%,  $p=0.004$ ). Hemodynamic data at eight different time points and biochemical data showed no differences between groups.

**Conclusions:** Patients receiving intrathecal sufentanil have more hemodynamical stability, as suggested by the reduced inotropic support and fewer adjustments in intravenous opioid doses.

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## Introduction

Intrathecal opioids in combination with general anesthesia reduce pain intensity and anesthetics consumption facilitating early removal of the endotracheal tube and improving postoperative analgesia in patients undergoing coronary artery bypass grafting (CABG) with cardiopulmonary bypass (CPB). Furthermore, they can decrease surgical stress response and have cardioprotective effects.<sup>1-5</sup> In CABG surgery, prevention of perioperative adverse events, such as tachycardia and myocardial infarction, is advisable. Hemodynamic stability and reduction of stress response contribute, in part, to reduce myocardial damage.<sup>1,6</sup>

Compared to morphine, intrathecal sufentanil provides faster and more intense analgesia.<sup>3,7</sup> In fact, because of morphine's lipid solubility, analgesic effects after intrathecal injection are delayed and only large intrathecal doses (10 mg) may initiate reliable intraoperative analgesia in this setting.<sup>3</sup> Besides that, some authors suggest that intrathecal sufentanil provides better hemodynamic stability when compared to other opioids.<sup>2,8</sup>

The aim of this study was to evaluate, for the first time, the hemodynamic effects of adding intrathecal sufentanil to general anesthesia in patients undergoing coronary artery bypass grafting with cardiopulmonary bypass.

## Methods

Ethical approval for this study (protocol number CEP 3458) was provided by the Ethical Committee CEP Instituto Dante Pazzanese of São Paulo, Brasil on 29 August 2006. After written informed consent we enrolled 40 patients scheduled to undergo elective CABG with CPB with two to four grafts, with one graft always being the left internal mammary artery and the others the safena magna vein.

Exclusion criteria were: chronic kidney disease; emergency procedures; reoperations; contraindication to spinal block according to 2002 American Society of Regional Anesthesia Consensus Conference<sup>9</sup>; left ventricular ejection fraction less than 40%; body mass index (BMI) above 32 kg/m<sup>2</sup> and use of nitroglycerin.

Patients were randomly assigned to two different anesthetic protocols (sufentanil group or control group) depending on receiving or not intrathecal sufentanil. A computer generated random table determined in which group patients were allocated. The participants' randomization assignment was concealed in an envelope until the last available moment (start of anesthesia).

Patients received their usual medications until the day of operation, with the exception of oral hypoglycemic agents, which were discontinued and/or replaced by insulin at least three days before surgery. All patients received 7.5 mg of midazolam intramuscularly 1 h before surgery.

Monitoring included continuous electrocardiography of the DII and modified V5, analysis of the ST segment in DII, DI and modified V5 derivations, pulse oximetry, invasive mean blood pressure (MAP) positioned in the radial artery, analysis of the bispectral index (BIS), capnography, blood gas analysis, temperature measurement at the lower third of the esophagus, urinary catheterization, assessment of neuromuscular function with TOF WATCH and evaluation of

hemodynamic data made with a pulmonary artery catheter (Swan-Ganz model, continuous output), positioned on the right subclavian vein (monitor Vigilance II®, Edwards Lifesciences, Irvine, CA, USA).

In sufentanil group, after initial monitoring, patients were placed in a sitting position and underwent lumbar puncture in the L3-L4 space with a 25 gauge Whitacre needle. After confirmation of puncture of the subarachnoid space, successful spinal was given to all these patients, 5 mL of saline solution 0.9% containing 1 µg/kg sufentanil (and never more than 100 µg) was injected over a 10 s period. General anesthesia was then initiated.

In control group, general anesthesia was initiated immediately after initial monitoring.

All patients underwent inhalation induction as follows: facial mask with using 2% sevoflurane in 100% oxygen and fresh gas flow of 6 L/min for 30 s. Inspired concentration of sevoflurane was then increased to 7% until loss of consciousness and then reduced to 2%. Next, intravenous infusion of remifentanyl began at a dose of 1 µg/kg for 1 min and 0.1 mg/kg pancuronium was administered 3 min before tracheal intubation. Volume-controlled ventilation was started with the following parameters: tidal volume 8-10 mL/kg, respiratory rate adequate to maintain end Tidal CO<sub>2</sub> between 30 and 35 mmHg and fresh gas flow of 2 L with 60% fraction of inspired oxygen mixed with compressed air.

The maintenance of anesthesia in the period before and after CPB was performed with sevoflurane in the expired fraction with variation between 0.5% and 2% to maintain the BIS between 40 and 65. Remifentanyl was administered at an infusion rate up to 0.4 µg/kg/min to maintain mean arterial pressure levels between 60 and 80 mmHg. A bolus of 0.02 mg/kg pancuronium was administered when the third response to the sequence of four stimuli appeared in the TOF WATCH monitor until the end of the procedure.

During CPB, anesthesia was maintained with sevoflurane at levels between 0.5% and 2% administered together with a mixture of oxygen and compressed air in the oxygenator circuit through calibrated vaporizer to maintain the BIS value between 40 and 65 and remifentanyl up to 0.4 µg/kg/min for control of mean arterial pressure between 45 and 70 mmHg.

Upon completion of the surgical procedure, all patients received a continuous intravenous infusion of 2 µg/kg/min propofol as a sedative and were transferred to the ICU, where they remained sedated for a 1-h period. The analgesia protocol was initiated within the first 24 h with a single intravenous dose of 1 µg/kg fentanyl together with 1 g of dypirone. The same dose of dypirone was repeated every 6 h.

After tracheal extubation, patient control analgesia (venous PCA) with a Vigon® PCA pump was then installed with the following parameters: bolus only mode, 1 mg bolus and a fixed 7-min lockout interval. During this period, if there was significant pain (VAS > 7), 100 mg of tramadol was administered intravenously. Discharge from the ICU and hospital were followed by local protocols.

Hemodynamic goals during anesthesia were maintenance of central venous pressure (CVP) and pulmonary capillary wedge pressure (PCP) between 8 and 12 mmHg with administration of crystalloids and colloids and maintenance of mean arterial pressure (MAP) between 60 and 80 mmHg.

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