

# INTRAVENOUS SUFENTANIL AND MORPHINE FOR POST-CARDIAC SURGERY PAIN RELIEF USING PATIENT-CONTROLLED ANALGESIA (PCA) DEVICE: A RANDOMIZED DOUBLE-BLIND CLINICAL TRIAL

Seyed Mostafa Alavi<sup>1</sup>, Rasoul Ferasat Kish<sup>2</sup>, Fariborz Farsad<sup>3</sup>,  
Farnad Imani<sup>4</sup>, Mehrdad Sheikhvatan<sup>5</sup>

## ABSTRACT

**Background:** Selection of the best analgesic technique in patients undergoing major surgeries can result in lower morbidity and satisfactory postoperative pain relief. In the present study, we tried to compare the effect of morphine and sufentanil on postoperative pain severity and hemodynamic changes by using patient-controlled analgesia (PCA) device in patients who were candidate for coronary artery bypass surgery (CABG).

**Methodology:** It was a randomized double-blinded clinical trial in which 120 patients aged 30-65 years, ASA physical status I-III, candidate for CABG in Shahid Rajaee hospital in Tehran were included. Before anesthesia, patients were randomly assigned to one of three groups to receive sufentanil (n=40), morphine (n=40) or normal saline (n=40). After tracheal extubation at intensive care unit, PCA was started by, sufentanil 4mg for the first group, morphine 2mg for the second group and normal saline, at same volume for the third group, intravenously with 10 minute lockout interval. Postoperative pain was evaluated by VAS scale, 1, 6, 12, 18 and 24 hours after extubation and systolic blood pressure, arterial oxygen saturation, PCO<sub>2</sub> and PO<sub>2</sub> were recorded 24 hours after extubation.

**Results:** VAS scores at rest revealed significantly less pain for patients in sufentanil and morphine groups than normal saline group, throughout the twenty-four hours after operation (P<0.001). However, there were no significant differences in the means of VAS scores between sufentanil and morphine groups. Among studied hemodynamic parameters, only systolic blood pressure was reduced more in morphine than sufentanil group (P<0.001).

**Conclusion:** After CABG surgery, administration of intravenous sufentanil and morphine using PCA can lead to similar reduction of postoperative pain severity.

**KEYWORDS:** Pain, Sufentanil, Morphine, Coronary artery bypass grafting.

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## Correspondence:

Seyed Mostafa Alavi,  
Iran University of Medical Sciences,  
P.O.Box: 13185-1678,  
Tehran, Iran  
Email: swt\_f@yahoo.com

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## INTRODUCTION

The use of optimal analgesics can provide intraoperative hemodynamic stability, significant postoperative analgesia and maximum patient's satisfaction. Therefore, selection of the best analgesic technique in patients undergoing major surgeries can result in lower

morbidity and shorter hospital stay. In low-risk patients undergoing coronary artery bypass graft (CABG) or valve surgery, the beneficial and side effects of some anesthetic agents such as sufentanil and morphine are questioned. Sufentanil is commonly used during anesthesia for patients undergoing cardiac surgery; however, this drug has a rapid onset and shorter duration of action. On the contrary, administration of morphine can lead to the long duration of action, but a slow onset of action.<sup>1</sup>

Some studies have indicated that intrathecal morphine can provide significant postoperative analgesia without delaying extubation after cardiac surgery.<sup>2</sup> Besides, it was hypothesized that sufentanil would provide improved intraoperative hemodynamic stability.<sup>3</sup> Moreover, some studies have demonstrated that after cardiac surgery, postoperative pain management with prolonged infusion of sufentanil adapted to a pain score during deep inspiration can achieve better analgesia during routine bedside procedures and higher pulmonary volumes than on-demand boluses of morphine.<sup>4</sup> However, some other investigators have showed that analgesic efficacy and side effects of epidural sufentanil and morphine were similar.<sup>5</sup> Thus, it seems that the available literature has not clearly compared the analgesic effects of both analgesics after cardiac surgery.

In the present study, our objective was to compare the analgesic effect of morphine, sufentanil and placebo on postoperative pain severity and hemodynamic changes by using patient-controlled analgesia (PCA) device in patients who undergo for CABG surgery.

## METHODOLOGY

It was a randomized double-blind clinical trial in which 120 patients aged 30-65 years old, ASA physical status I-III, candidate for CABG in Shahid Rajaei hospital in Tehran were included. The study was approved by the Educational Hospital Ethics Committee, governing the participation of human subjects in research at the Iran University of Medical Sciences, according to the principles outlined in the Declaration of Helsinki. The procedure and type

of anesthetics were explained to patients, and written informed consents were obtained from all the patients before injection of local anesthetics. Emergency patients and who underwent other cardiac and non-cardiac procedures were excluded. Also, excluded were the patient with renal or hepatic failure, diabetic neuropathy, low ejection fraction (<30%), or need for intra-aortic balloon pump.

One day before the operation, patients received instructions about the use of a patient-controlled analgesia (PCA) device (Pain Management Provider) and the visual analog scale (VAS) for pain. This scale consisted of an unmarked 10-mm line on which 0 mm represents no pain and 10 mm represents the worst pain imaginable. Before anesthesia, patients were randomly assigned to one of three groups to receive sufentanil (group S, n=40), morphine (group M, n=40) or normal saline (group NS, n=40). All patients and laboratory staff were blinded to the treatment allocation. Preoperatively, patients were given lorazepam, 0.02-0.03 mg/kg orally, night before and two hours before surgery and also morphine, 0.1 µg/kg intravenously, one hour before operation. General anesthesia was induced with 1-1.5 mg/kg propofol and 1 µg/kg remifentanyl. A radial artery catheter was placed and tracheal intubation with a double-lumen tube was facilitated by 0.5 mg/kg vecuronium. Anesthesia was maintained with 50-100 µg/kg/min propofol and 0.1 µg/kg/min remifentanyl.

Anesthesia was targeted to allow tracheal extubation in the operating room immediately after the surgical procedure and after fulfilling standard extubation criteria. The patients' were extubated if central temperature was ~36°C and if the patients were cardiovascularly stable. After extubation at intensive care unit, PCA was started by morphine 2mg for group M, Sufentanil 4mg for group S and normal saline, at same volume for group NS with 10 minute lockout interval. Postoperative pain was evaluated by VAS scale, 1, 6, 12, 18 and 24 hours after extubation. When VAS scale was more than 5, morphine 3-5 mg bolus at 5 minutes intervals) was administered intravenously. Systolic blood

Table-I: Demographic characteristics and clinical data of studied patients

Item	Sufentanil group (n=40)	Morphine group (n=40)	Normal Saline group (n=40)	P value
Male gender	17 (42.5)	22 (55.0)	22 (55.0)	0.434
Weight (kg)	73.8±7.4	72.6±7.9	73.7±7.4	0.708
Age (year)	59.1±7.1	59.3±8.6	59.1±8.6	0.992
Operation time (min)	333.0±23.5	333.7±26.3	339.6±21.8	0.403
CPB time (min)	87.6±9.8	88.3±10.8	87.3±11.3	0.914

CPB: Cardio-Pulmonary Bypass

Data are presented as mean ± SD or number (percentage)

pressure, Arterial oxygen saturation, PCO<sub>2</sub> and PO<sub>2</sub> were recorded 24 hours after extubation. Results were reported as mean ± standard deviation (SD) for quantitative variables and percentages for categorical variables. The groups were compared using One-way analysis of variance test (ANOVA) for continuous variables and the chi-square test or Fisher's exact test if required for categorical variables. P values of 0.05 or less were considered statistically significant. All the statistical analyses were performed using SPSS version 13.0 (SPSS Inc., Chicago, IL, USA) for Windows.

## RESULTS

Demographic characteristics and clinical data are shown in Table 1. The three groups had similar baseline characteristics. The durations of surgery and cardiopulmonary bypass were similar in three groups.

VAS scores at rest revealed significantly less pain for patients in sufentanil and morphine groups than normal saline group, throughout the twenty-four hours after operation (P<0.001). However, there were no significant differences in the means of VAS scores between sufentanil and morphine groups (Figure-1).

In the terms of hemodynamic parameters, there were no significant differences in the mean of PCO<sub>2</sub>, PO<sub>2</sub> and arterial O<sub>2</sub> saturation of patients, 24 hours after extubation, whereas, systolic blood pressure was reduced more in morphine than sufentanil group and this parameter was lower in above both groups than control group (P<0.001).

## DISCUSSION

The use of PCA technique is an effective procedure, especially for postoperative pain relief. The efficacy of this technique is fundamentally based on the beginning of PCA after patient's loading with intravenous opioids till a successful pain relief in patients is obtained. Some studies have demonstrated the high influence of PCA technique on the quality of analgesia and postoperative pain management. Gust et al. found that the patients treated with PCA experienced a higher quality of analgesia and this technique reduced respiratory complications after coronary artery bypass grafting.<sup>6</sup> Also, in a study by Searle et al. it was indicated that the day-to-day VAS pain score decreased in the PCA group, while it remained unchanged in patients who treated with conventional

Table-II: Hemodynamic parameters, 24 hours after extubation in studied groups

Item	Sufentanil group (n=40)	Morphine group (n=40)	Normal Saline group (n=40)	P value
PCO <sub>2</sub> (mmHg)	38.1±2.1	37.7±1.5	40.0±1.8	0.091
PO <sub>2</sub> (mmHg)	109.8±9.7	113.9±9.2	106.3±9.9	0.063
SaO <sub>2</sub> (%)	97.3±1.4	97.9±1.7	97.4±1.2	0.169
SBP (mmHg)	114.5±8.8	110.5±6.9	132.5±12.2	<0.001

Data are presented as mean ± SD

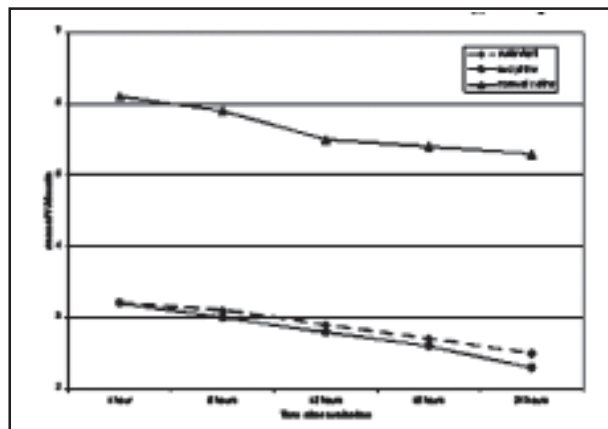


Figure-1: Comparative mean VAS scale over time for sufentanil, morphine and normal saline group.

analgesic therapy. Furthermore, they showed that the PCA patients had lower VAS pain scores at extubation than other studied group.<sup>7</sup> In addition, in another study by Boldt et al. pain management using PCA systems recommended for cardiac surgery patients and it appeared to be superior to standard nurse-based pain therapy.<sup>8</sup>

In the present study and on the basis of using PCA technique for postoperative pain management, although the means of VAS scores between the two interventional groups were significantly higher than the group administered normal saline, these scores were similar between sufentanil and morphine groups. Previous studies had different findings. In a study by Aubrun et al. for the determination of Predictive factors of severe postoperative pain in the postanesthesia care unit, a higher intraoperative dose of sufentanil, has been shown as a main predictor for severe postoperative pain.<sup>9</sup> However, in another study by Bastin et al. it was indicated that postoperative pain management after cardiac surgery with infusion of sufentanil adapted to a pain score during deep inspiration could achieve better analgesia during routine bedside procedures and higher pulmonary volumes than on-demand boluses of morphine.<sup>4</sup>

Furthermore, in a similar study by Kazemi et al. on patients undergoing arthroscopic knee surgery, although the injection of morphine and sufentanil could reduce both the post

arthroscopic knee procedures pain and the need for supplementary analgesics; however, sufentanil was more effective than morphine.<sup>10</sup> Moreover, Liu et al. showed that combined sufentanil and morphine provided superior postoperative pain relief both at rest (11 h) and on coughing (8 h) than did IV patient-controlled analgesia morphine alone.<sup>11</sup> It seems that according to the rapid onset of sufentanil and long duration of action of morphine, concomitant use of these two analgesics can be recommended so that the efficacy of concurrent administration of these two drugs has been reported in some previous studies.<sup>1,12,13</sup>

We also evaluated and compared the hemodynamic changes after the administration of sufentanil and morphine and found that although most of the hemodynamic indices were induced 24 hours after extubation, but the reduction of systolic blood pressure in morphine group was more severe than sufentanil group. Similarly, in a study by Flacke et al, due to increases in blood pressure to greater than 15% above control values, supplementation with a potent inhalational agent was necessary in 30% of the patients given, whereas no sufentanil patient required supplementation.<sup>14</sup> Furthermore, in Ionescu et al. study, the fall in systemic pressure and left ventricular work occurred in the groups that were administered sufentanil and morphine after induction of general anesthesia. However, this reduction was more evident after revascularization in the group administered morphine.<sup>15</sup> Moreover, Stanford showed that sufentanil allowed more rapid induction, earlier emergence from anesthesia, and faster extubation of patients than either morphine.<sup>16</sup> Another study has showed that the hemodynamic changes of sufentanil are transient and sufentanil anesthesia provides good cardiovascular stability for cardiac surgery.<sup>17</sup> Total reduction in systemic pressure and left ventricular work in both groups after induction of general anesthesia suggests that sufentanil and morphine must be used with caution in patients with hypovolemic or cardiovascular disease and this notice must be considered in morphine group.

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### Authors:

- Seyed Mostafa Alavi
- Rasoul Ferasat Kish
- Fariborz Farsad
- Farnad Imani
- Mehrdad Sheikhatvan
- 1-5: Iran University of Medical Sciences, Tehran - Iran.