Haemodynamic stability with midazolam-ketamine-sufentanil analgesia in cardiac surgical patients

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Although sufentanil in high doses may result in deep coma sufficient to conduct coronary-bypass surgery painlessly in patients, its side effects, e.g., bradycardia and hypotension, may lead to complications in some patients. Since ketamine causes central sympathetic stimulation, we attempted to counteract the vagomimetic effects of sufentanil by ketamine. Anaesthesia was induced in patients, (n = 15), for elective coronary artery-bypass surgery with 0.12 mg · kg^{-1} midazolam IV, followed by 1 mg · kg^{-1} ketamine and 0.6 μg · kg^{-1} sufentanil IV eight minutes later. Subsequently, pancuronium 0.1 mg · kg^{-1} was given to facilitate tracheal intubation. Three minutes later, the trachea was intubated, and ketamine 1 mg · kg^{-1} · hr^{-1} IV infusion was started. Incremental doses of 0.6 μg · kg^{-1} sufentanil were given whenever a greater than 15 per cent increase in rate-pressure product was observed. The mean ± S.E.M. dose of sufentanil before cardiopulmonary bypass was 6.5 ± 0.6 μg · kg and 9.1 ± 0.9 μg · kg for the entire procedure. Although midazolam alone caused reductions in systolic BP, SVR and LVSWI, other haemodynamic variables were not altered. The administration of this anaesthetic technique caused no clinically important adverse haemodynamic changes and/or ST-segment changes and prevented the adverse haemodynamic changes caused by intubation, skin incision, sternotomy and periaortic dissection. Adequate analgesia, complete amnesia and early recovery of wakefulness were observed.

Key words

ANAESTHESIA: cardiac; ANAESTHETICS, INTRAVENOUS: ketamine, sufentanil; HYPNOTICS: benzodiazepines, midazolam; ANALGESICS: sufentanil; ketamine; BLOOD PRESSURE: drug effects; SURGERY: cadiac.

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Sufentanil has a well established effectiveness for analgesia in cardiac surgical patients,[1] although bradycardia and hypotension associated with high IV doses of sufentanil may prevent its use in patients prone to bradycardia.[2] Since ketamine causes sympathetic and sufentanil causes parasympathetic stimulation, it seems rational to utilize this analgesic-amnesic drug combination for balanced anaesthesia for cardiac surgery in order to maintain a stable haemodynamic condition free from excessive autonomic stimulation caused by stress-inducing events, e.g., skin incision, intubation or sternotomy. Ketamine, however, causes marked central sympathetic stimulation resulting in increases in heart rate (HR), blood pressure (BP) and rate-pressure product (RPP), hence it could precipitate myocardial ischaemia by increasing myocardial oxygen demand in patients with limited coronary blood supply.[3–5] Therefore, the injection of 1–2 mg · kg^{-1} ketamine at a rapid rate without pretreatment with benzodiazepines in cardiac patients is contraindicated. Diazepam has been shown to block the adverse haemodynamic and endocrine effects of ketamine in cardiac surgical patients.[6–8] However, no information is available about the effectiveness and safety of midazolam, its congener, in combination with ketamine in cardiac patients despite the established safety of midazolam-ketamine induction sequence in non-cardiac patients.[9] Although ketamine has been used in intravenous infusion in healthy ASA physical status I–II patients, burn patients[10,11] and paediatric cardiac surgical patients,[12] little information is available on its safety in adult cardiac surgical patients. Therefore, this study was undertaken to determine the following: (1) whether midazolam is as effective as diazepam in preventing ketamine-induced sympathetic stimulation; (2) whether the combination of ketamine with sufentanil leads to haemodynamic stability

during intubation; (3) whether ketamine IV infusion with intermittent sufentanil supplementation is effective and safe for maintenance of anaesthesia for coronary bypass surgery.

Methods

Fifteen patients scheduled to undergo elective aorto-coronary artery bypass graft surgery were studied. Patients with a history of drug habituation or addiction, psychiatric treatment, or allergic reactions to narcotic-analgesic drugs were excluded. Patients who were undergoing emergency surgery or who were minors or prisoners were also excluded. The patients were selected at random from consecutive surgical procedures. A valid written informed consent, as required by the Institutional Research Review Board, was obtained prior to the study. Patients were maintained on β-blockers or calcium channel blockers until the time of anaesthetic induction. The morning digoxin was withheld.

The night prior to surgery, the patients received a benzodiazepine hypnotic, usually triazolam 0.25 mg PO, for sleep. For preoperative preparations, each patient received diazepam 0.15 $mg \cdot kg^{-1}$ PO and morphine sulfate 0.15 $mg \cdot kg^{-1}$ IM 60 minutes prior to induction.

Monitoring

In the preoperative preparation area, an IV line was established. An arterial plastic cannula was inserted into a radial artery under local anaesthesia. A balloontipped pulmonary artery catheter was placed into the pulmonary artery through an introducer previously inserted percutaneously into the right internal jugular vein. The ECG lead II and V_5 and blood pressure, by a non-invasive monitor*, were monitored continuously in the preoperative preparation area until the patients were transferred to the operating room. In the OR, direct arterial systemic pressure, pulmonary artery pressure and ECG were recorded on a multichannel monitor linked to a computer terminal. Oxygen saturation was measured continuously by an oximeter and maintained at > 95 per cent saturation. Exhaled CO_2 was displayed and continually recorded by a capnograph in order to assure that CO_2 level was between 35 and 45 mmHg. Tidal volume and ventilatory rate were monitored by a respirometer. Blood gases were determined at each blood sampling and whenever indicated. Cardiac output was determined in triplicate by thermodilution with a cardiac output computer. The ECG was continuously monitored in leads II and V_5 for any ST-segment changes for statistical analysis. The changes were evaluated by an independent cardiologist unaware of the type of surgery or the times the readings were taken.

*Dinamap, Critikon Inc., Tampa, FL.

Haemodynamic data were determined and calculated at the times before and throughout anaesthesia and surgery as shown in Tables I and II.

The results five minutes after skin incision were considered as values prior to sternotomy, since the time interval between skin incision and sternotomy was short, and data were available only for five minutes in all patients.

Haemodynamic variables evaluated were:

- Heart rate (HR)
- Systolic systemic blood pressure: (BP_s) mmHg
- Diastolic systemic blood pressure: (BP_d) mmHg
- Pulmonary artery systolic blood pressure:(PAP_s)mmHg
- Pulmonary artery diastolic blood pressure:(PAP_d)mmHg
- Pulmonary artery wedge pressure: (PAP_w) mmHg
- Central venous pressure (CVP): cmH_2O
- Cardiac output (CO): $L \cdot min^{-1}$

The following haemodynamic data were calculated:

- Cardiac index (CI): $L \cdot min^{-1} \cdot m^{-2}$
- Stroke volume (SV): ml
- Stroke index (SI): $ml \cdot m^{-2}$
- Left ventricular stroke work index (LVSWI): $g\text{-}m \cdot m^{-2}$
- Right ventricular stroke work index (RVSWI): $g\text{-}m \cdot m^{-2}$
- Systemic vascular resistance (SVR): $dynes \cdot sec \cdot cm^{-5}$
- Pulmonary vascular resistance (PVR): $dynes \cdot sec \cdot cm^{-5}$
- Rate pressure product (RPP): HR × BP_s

Anaesthetic management

A tranquil state and amnesia were induced by midazolam in a mean ± SEM dose 0.12 ± 0.01 $mg \cdot kg^{-1}$ given IV over one minute to the patients who were spontaneously breathing 100 per cent O_2. Eight minutes after the end of midazolam infusion, the IV injection of a loading dose of 1 ± 0.3 $mg \cdot kg^{-1}$ ketamine was given over one minute followed by 0.6 $\mu g \cdot kg^{-1}$ sufentanil. One minute later, pancuronium bromide 0.1 $mg \cdot kg^{-1}$ IV was given. Three minutes later, intubation was carried out without spraying the vocal cords with a local anaesthetic. After confirming the correct position of the tracheal tube, 100 per cent oxygen or oxygen in air was administered at an FiO_2 to maintain > 95 per cent oxygen saturation. None of the patients received N_2O. Ketamine IV infusion was started at the rate of 1 $mg \cdot kg^{-1} \cdot hr^{-1}$ after the completion of tracheal intubation. Additional incremental doses of 0.6 $\mu g \cdot kg^{-1}$ sufentanil were given based on the greater than 15 per cent increase in RPP. Additional doses of midazolam were injected when eye-signs of pain or awareness and other clinical evidence of increased sympathetic activity showed inadequate analgesia or possible awareness of events. Pancuronium in intermittent doses was given throughout anaesthesia based on the response of the thumb to ulnar nerve stimulation whenever required. Throughout the study, until cardiopulmonary bypass, the

TABLE I Haemodynamic changes

Haemodynamic measurements	*Before induct.*	*After midazo.*	*Before intub.*	*1' After intub.*	*5' After intub.*	*10' After intub.*	*Before skin incision*
BPs mmHg	136.4 ± 5.4	116.8 ± 5.1†	113.4 ± 3.9†	116.0 ± 2.8†	114.1 ± 3.1†	119.4 ± 3.5†	127.3 ± 3.0
BPd mmHg	66.5 ± 2.6	60.9 ± 2.9	59.1 ± 2.4*	63.8 ± 2.3	63.7 ± 2.1	64.8 ± 2.6	69.7 ± 2.4
HR beats·min^{-1}	66.0 ± 3.0	71.2 ± 3.0	74.0 ± 2.8	76.6 ± 2.8*	76.0 ± 2.7*	77.1 ± 3.2*	72.1 ± 3.5
PAPs mmHg	30.2 ± 3.0	33.0 ± 2.9	32.6 ± 2.6	30.7 ± 2.4	29.9 ± 2.2	29.5 ± 2.2	27.7 ± 2.1
PAPd mmHg	14.1 ± 1.1	15.9 ± 1.2	16.3 ± 1.4	17.1 ± 1.2	16.7 ± 1.0	15.7 ± 1.1	15.8 ± 1.1
CO L·min^{-1}	4.8 ± 0.3	4.8 ± 0.3	5.0 ± 0.3	4.9 ± 0.2	4.8 ± 0.2	4.9 ± 0.2	4.9 ± 0.2
CI L·min^{-1}·m^{-2}	2.4 ± 0.1	2.5 ± 0.1	2.5 ± 0.1	2.4 ± 0.1	2.4 ± 0.1	2.5 ± 0.1	2.5 ± 0.1
SI ml·m^{-2}	37.0 ± 1.4	35.0 ± 1.5	34.5 ± 1.5	32.5 ± 1.1*	32.3 ± 1.1*	32.7 ± 1.3*	36.0 ± 2.0
SVR dynes·sec·cm^{-5}	1391.9 ± 62.9	1199.4 ± 66.0*	1128.5 ± 62.3†	1232.4 ± 56.2	1211.0 ± 57.4*§	1227.2 ± 63.5	1318.4 ± 54.7
PVR dynes·sec·cm^{-5}	134.3 ± 22.7	174.0 ± 30.6	184.6 ± 25.6	178.6 ± 25.6	162.7 ± 22.3	139.7 ± 17.1	127.8 ± 18.8
LVSWI g-m·m^{-2}	39.4 ± 2.4	32.1 ± 2.0*	31.0 ± 1.6†	33.2 ± 1.7*	31.9 ± 1.1†	31.4 ± 1.2†	37.8 ± 2.6
RVSWI g-m·m^{-2}	9.7 ± 0.8	9.9 ± 0.7	9.9 ± 0.8	10.0 ± 0.9	9.3 ± 0.6	8.8 ± 0.5	9.4 ± 0.7

* $P < 0.05$ Compared with the before induction values.
† $P < 0.01$
‡ $P < 0.05$ Compared with the after midazolam values.
§ $P < 0.01$

patients required no IV infusion of vasopressors and/or vasodilators, β-blocker or Ca-channel blocker IV injections. After cardiopulmonary bypass, vasopressors and/or vasodilators were given occasionally as required.

During the postoperative period, the following were recorded: the investigator's evaluation of the procedure based on the review of complications, such as episodes of dysrhythmias, hypo- or hypertension, bronchospasm, hypersecretion on induction, and maintenance (excellent, good, fair, poor); time to recovery of spontaneous respiration, and to the first analgesic administration, amnesia on a scale: complete, partial, none; recall for intraoperative events or pain. The patients were observed for hallucinations and interviewed for bad dreams, illusions or distortion of body image and adequacy of anaesthesia on a scale (excellent, good, fair, poor).

Data analysis

The haemodynamic variables were evaluated for a change from the baseline at each sampling time during the procedure, using the ANOVA and SAS program. Baseline was defined in two ways: as preinduction and as post-midazolam. Statistical significance was defined at $P \leq 0.05$. All values are expressed as mean ± SEM.

Results

All patients were male. The mean age was 58.9 ± 2.2 yr, mean weight was 79.5 ± 4.5 kg, and mean height was 175.9 ± 2.3 cm, with mean BSA 1.97 ± 0.1 m^2. Their mean ejection fraction was 0.45 ± 0.05 (range from 0.29 to 0.60).

Intravenous injection of midazolam caused significant reductions in BP_s, SVR and LVSWI, but no concomitant changes in other directly measured and calculated haemodynamic variables (Tables I and II).

The injection of ketamine 1 mg·kg^{-1} in combination with 0.6 μg·kg^{-1} dose of sufentanil caused a decrease in BP_d and further decreases in SVR and LVSWI. After

TABLE II Haemodynamic changes

Haemodynamic measurements	*5' After skin incision*	*1' After sterno.*	*5' After sterno.*	*10' After sterno.*	*Before bypass*	*After bypass*	*End of procedure*
BPs mmHg	126.8 ± 2.5	131.7 ± 2.0‡	129.7 ± 1.8‡	128.7 ± 2.5‡	116.3 ± 2.6†	116.7 ± 2.1†	113.6 ± 7.7†
BPd mmHg	68.6 ± 2.2‡	73.0 ± 2.0§	69.8 ± 1.8‡	70.3 ± 2.1§	62.7 ± 1.5	60.5 ± 4.2	63.9 ± 2.2
HR beats·min^{-1}	71.3 ± 3.2	74.5 ± 3.4	71.7 ± 2.6	69.3 ± 3.0	72.1 ± 3.8	85.5 ± 2.7†§	85.1 ± 3.0†§
PAPs mmHg	27.2 ± 1.9	28.3 ± 1.9	27.8 ± 1.8	25.7 ± 2.2‡	26.1 ± 3.2	24.9 ± 2.1‡	24.6 ± 1.6‡
PAPd mmHg	15.7 ± 0.9	17.3 ± 1.0	15.7 ± 0.8	13.5 ± 1.2	14.7 ± 1.8	13.7 ± 1.4	13.8 ± 1.1
CO L·min^{-1}	4.8 ± 0.2	4.7 ± 0.2	4.6 ± 0.2	4.7 ± 0.2	4.5 ± 0.3	5.3 ± 0.3	5.2 ± 0.1
CI L·min^{-1}·m^{-2}	2.4 ± 0.1	2.4 ± 0.1	2.4 ± 0.1	2.4 ± 0.1	2.3 ± 0.1	2.7 ± 0.2	2.7 ± 0.1
SI ml·m^{-2}	35.0 ± 1.7	32.8 ± 1.5*	33.6 ± 1.8	35.3 ± 2.4	32.6 ± 1.9	32.3 ± 2.1	31.4 ± 1.1
SVR dynes·sec·cm^{-5}	1341.7 ± 54.9	1467 ± 54.9§	1422.8 ± 48.9§	1372.9 ± 53.7‡	1331.5 ± 96.1	1103.8 ± 84.5†	1133.6 ± 35.3†
PVR dynes·sec·cm^{-5}	126.8 ± 19.1	162.3 ± 26.4	137.3 ± 22.1	97.5 ± 19.3‡	141.5 ± 46.6	103.6 ± 30.4	95.1 ± 16.5
LVSWI g-m·m^{-2}	37.9 ± 2.0‡	38.4 ± 2.1	37.5 ± 2.3	38.5 ± 2.7	30.7 ± 2.0†	29.4 ± 1.7†	30.4 ± 1.0†
RVSWI g-m·m^{-2}	9.1 ± 0.7	9.2 ± 0.6	9.0 ± 0.6	8.5 ± 0.9	8.0 ± 0.9	7.5 ± 0.8*	7.5 ± 0.6*‡

* $P < 0.05$ Compared with the before induction values.
† $P < 0.01$
‡ $P < 0.05$ Compared with the after midazolam values.
§ $P < 0.01$

tracheal intubation, no significant changes in BP_s or BP_d were observed compared with pre-intubation values. Additional haemodynamic changes compared with preinduction values following tracheal intubation were as follows: increase in HR, decrease in SI, and marked decreases in BP_s and LVSWI (Table I).

Following skin incision at sternotomy and after sternotomy, the haemodynamic variables were not significantly different from preinduction values (Table II). No significant changes in any of the haemodynamic variables were observed pre- vs post-incision and pre- vs post-sternotomy. Nor were there significant changes in any measured haemodynamic variables after sternotomy observed compared with the preinduction values (Table II).

Before the initiation of cardiopulmonary bypass, significant reductions in BP_s and LVSWI were observed (Table II). Following the termination of cardiopulmonary bypass, marked reductions in BP_s, SVR and LVSWI were sustained until the end of the operation; whereas the HR remained significantly elevated compared with either preinduction or prebypass values to the end of operation in the entire postbypass period (Table II).

Maintenance of anaesthesia until cannulation for cardiopulmonary bypass was free of complications, such as episodes of arrythmias, ST-segment changes, brady- and/or tachycardia, hypo- or hypertension, bronchospasm, hypersecretion on induction and/or maintenance The quality of anaesthesia, based on the haemodynamic stability, was rated excellent in 13 patients and good in two. No recall of pain was reported in any patient on postoperative interviews: 12 patients rated their anaesthetic experience as excellent and three patients as good. The time interval to the first analgesic administration was less than one hour. No patients had any recall of intraoperative events and/or operative and/or anginal pain. Therefore, amnesia was rated as complete in all patients. No hallucinations, illusions, bad dreams or distortion of body image were reported in any of the patients.

No ECG changes indicating myocardial ischaemia or

infarct were detected from the time of anaesthetic induction until cardiopulmonary bypass. No pulmonary oedema or heart failure occurred in any patients during the study period.

Recovery from anaesthesia was uneventful. The mean duration of anaesthesia from induction to the end of surgery was 383.0 ± 21 min. The mean interval from the end of anaesthesia to recovery of wakefulness was 118.0 ± 31.2 min; time to the first analgesic administration 53.4 ± 30.0 min. The total dose of sufentanil was 9.1 ± 0.9 $\mu g \cdot kg^{-1}$. Of this dose, 6.5 ± 0.6 $\mu g \cdot kg^{-1}$ was used before cardiopulmonary bypass, and 2.6 ± 0.4 $\mu g \cdot kg^{-1}$ was used post-bypass.

Discussion

This is the first report of the successful use of the combination of midazolam-ketamine-sufentanil as amnesicanalgesic components for both induction and maintenance of balanced anaesthesia in cardiac surgical patients. The lack of clinically important adverse haemodynamic changes with the use of this technique until cardiopulmonary-bypass proved the safety of our approach. Although the heart rate changes showed a significant increase after intubation compared with the preinduction values, but not if compared with the results after midazolam or before intubation.

The haemodynamic changes with midazolam-ketamine induction of anaesthesia are almost identical with those observed earlier with diazepam-ketamine.[7,13,14] Midazolam caused significant reductions in BP_s and SVR, just as with diazepam. Since a marked initial reduction in HR caused by diazepam was observed in earlier studies with diazepam-ketamine[7,13,14] but was not observed with midazolam in the present study, it is likely that this difference was due to the fact that our patients had been treated with long-acting β-blockers and Ca-channel blockers as evidenced by the preinduction HR of 66 ± 3.0. Since the baseline HR was slow, midazolam caused less slowing in HR than in patients who received treatment with the only available short-acting β-blocker, propranolol in the previous studies, which was also manifested in their preinduction HR of 82 ± 17.6[7] bpm. Evidently, the baseline autonomic tone was more markedly attenuated in our patients by the β-blockers of newer vintage. Therefore, one would expect less reduction in HR in the current study group than in the earlier studies following induction of anaesthesia. Nonetheless, the reduction in SVR and LVSWI following diazepam and midazolam reflects attenuation of central sympathetic activity. This was also reflected in the marked reduction of plasma-free epinephrine levels following diazepam in all the previous studies.[7,13,15]

The reduction in sympathetic autonomic activity, namely decreased SVR and BP_s or reduced afterload, benefits patients with limited coronary blood supply, since it leads to a reduction in left ventricular work load. This was reflected in the reduced LVSWI. These beneficial effects of benzodiazepines were earlier observed by Samuelson *et al.*[16] and Fragen *et al.*[17] in critically ill cardiac surgical patients with increased left ventricular end-diastolic pressure.

The haemodynamic changes following the sequential administration of midazolam-ketamine demonstrated protection from ketamine induced central sympathetic stimulation by prior injection of midazolam which was identical to that afforded by diazepam. Although ketamine alone causes marked increases in HR, B_s, BP_d, RPP, SVR, PAP_s, CO, CI, SV, SI, LVSWI and RVSWI, on the contrary in our studies, LVSWI and SVR were significantly reduced after midazolam-ketamine administration (Table I). In addition, no changes in cardiac output, stroke volume or PAP_s were found. As a result of these haemodynamic changes, it is likely that myocardial O_2 demand was also decreased. These results paralleled those observed earlier with a diazepam-ketamine induction sequence.[11,13,14] Ketamine utilized in the present study and the protection of patients from sympathetic stimulation by the β-blockers might have further contributed to the haemodynamic stability.

Haemodynamic changes following intubation were: a clinically unimportant, but statistically significant, increase in HR compared with the preinduction HR, but not with pre-intubation HR (Table I). However, no adverse but rather favourable haemodynamic changes were observed, namely a significant reduction in LVSWI and SI, when compared either with the pre- or post-intubation values.

Haemodynamic changes after skin incision or before sternotomy did not occur in comparison with either the baseline or the after midazolam values (Tables I and II). Significant haemodynamic changes following sternotomy compared with preinduction values were not observed. However, increase in BP_s, HR and SVR were significantly increased following sternotomy as compared with the after midazolam values (Tables I and II). Haemodynamic changes before cardiopulmonary bypass were: a further reduction of BP_s compared with the baseline and a reduction in LVSWI (Table II). Further reductions in LVSWI, RVSWI and SVR were maintained until the end of anaesthesia in the post-bypass period. However, in the post-bypass period, HR was significantly increased compared with either preinduction or after-midazolam values (Table II). Vasopressor drugs given in the post-bypass period might have contributed to this increase in HR.

Haemodynamic changes, in response to the three stressful events: tracheal intubation, skin incision and

sternotomy, have clearly demonstrated the safety of the sequential administration of midazolam-ketamine-sufentanil. We emphasize that the sufentanil dosages were less than those employed in the high-dose sufentanil-technique widely used.[2] Moreover, there was a 50 per cent reduction in the dose requirement of sufentanil when combined with ketamine in this study compared with the use of midazolam-sufentanil combination published in our earlier report in this journal.[1] Evidently ketamine reduced the sufentanil dose requirements as expected and ketamine and sufentanil with opposing autonomic effects balanced out the excessive autonomic activity. The lack of adverse occurrences intraoperatively, such as hypo- and hypertension, brady- or tachycardia, arrhythmias, ST-segment depression or myocardial infarct, further proves the safety of this anaesthetic technique. The contribution to the haemodynamic stability of long-acting β-blockers and/or Ca-channel blockers cannot be denied. Complications associated with high-dose fentanyl or sufentanil, chest wall rigidity, sudden bradycardia and hypotension, leading to myocardial ischaemic changes and/or myocardial infarct intraoperatively, severe hypotension necessitating the use of vasopressors, longer time period for weaning the patients from the ventilator were not observed with our anaesthetic technique.[2,5]

No recall of pain or any unpleasant experiences were reported in our patients on postoperative interviews. Postoperative return of wakefulness and orientation were acceptably prompt. None of the patients received naloxone or nalbuphine, since the tracheas of our patients remained intubated overnight as is routinely done postoperatively in our cardiac surgical patients.

In conclusion, a midazolam-ketamine-sufentanil-pancuronium-O_2 induction/intubation sequence caused no adverse haemodynamic changes in cardiac patients in the doses and sequences utilized in our study. Tracheal intubation, skin incision and sternotomy, the most stressful events, elicited no adverse haemodynamic effects. The use of ketamine for supplementation allowed a reduction in sufentanil requirements while it did not alter haemodynamic stability. Adequate pain relief, lack of recall of pain or other intraoperative events, patient satisfaction and good operating conditions were provided by this anaesthetic technique.

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Résumé

Même si la sufentanil à haute dose peut amener un coma profond suffisant pour une chirurgie coronarienne sans douleur chez les patients, les effets secondaires, tels que bradycardie et hypotension peuvent amener des complications. Etant donné que la kétamine provoque une stimulation sympathique centrale on a tenté de contrecarrer les effets vagomimétiques du sufentanil par la kétamine. L'anesthésie fut induite chez les patients (n = 15) se présentant pour chirurgie coronarienne élective avec 0.12 mg · kg^{-1} midazalam suivi de 1 mg · kg^{-1} de kétamine et 0.6 μg · kg^{-1} de sufentanil huit minutes plus tard. Par la suite du pancuronium 0.1 mg · kg^{-1} a été administré afin de faciliter l'intubation endotrachéale. Trois minutes plus tard la trachée fut intubée et la kétamine 1 mg·kg^{-1}·hr^{-1} en perfusion fut commencée. Des doses supplémentaires de 0.6 μg · kg^{-1} de sufentanil ont été administrées si le produit de la fréquence × pression augmentait de 15 pour cent. La dose moyenne de sufentanil avant la circulation extra corporelle était de 6.5 ± 0.6 μg · kg et 9.1 ± 0.9 μg · kg pour toute la procédure. Même si le midazolam seul a amené une diminution de la pression systolique, la résistance vasculaire systémique es de LVSWI, les autres données hémodynamiques ne furent pas altérées. L'administration de cette technique anesthésique n'a pas amené les altérations hémodynamiques clinique ou des altérations du segment-ST et a prévenu des changeéments hémodynamiques adverses lors de l'intubation, l'incision, la sternotomie et la dissection periaortique. Une analgésie adéquate, une amnésie complète et un réveil précoce furent observés.