The Effect of Primary Bolus Dose of Pancuronium versus Cisatracurium without Maintenance Dose on Extubation Time in Adult Coronary Artery Bypass Grafting

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Abstract

Background- Given the importance of the effect of muscle relaxants on the extubation time in coronary artery bypass grafting (CABG) patients, we sought to assess the difference in "time to extubation" and "intensive care unit (ICU) length of stay" between the primary bolus doses of Pancuronium and Cisatracurium without using the maintenance dose of them during surgery.

Methods- This double blind clinical trial divided 110 patients into two equal groups receiving either Cisatracurium or Pancuronium. The patients' surgical and cardiopulmonary bypass variables were evaluated, and the extubation time and ICU length of stay were compared between the two groups.

Results- There was no difference between the two groups regarding the depth of anesthesia, train-of-four (TOF) scores at the beginning of anesthesia, and the surgical and cardiopulmonary bypass variables. However, the Cisatracurium patients were extubated earlier and had a shorter ICU length of stay than the Pancuronium patients.

Conclusion- An appropriate depth of anesthesia facilitates the administration of the induction dose of Cisatracurium, which confers earlier extubation and shorter ICU length of stay by comparison with Pancuronium ***(Iranian Heart Journal 2011; 12 (1):22 -26).***

Keywords: coronary artery bypass grafting ■cisatracurium■ pancuronium■extubation

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One of the principal postoperative concerns in patients undergoing cardiac surgery is the time interval between patient entry to the intensive care unit (ICU) and extubation. This is primarily influenced by the anesthetic agents

as well as the induction and maintenance doses of muscle relaxants administered.
Coronary artery bypass grafting (CABG) is a relatively lengthy procedure and thus requires a sizable amount of muscle relaxants not only

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mild to moderate hypothermia, which can itself reduce the required dose of anesthetic agents. It may, therefore, be possible to administer the minimum dose of muscle relaxants necessary to effect acceptable (not full) levels of muscle relaxation, such that the patient's minimal diaphragmatic movements can be neglected by the anesthesiologist and the surgeon with a view to an earlier extubation and shorter length of ICU stay.
The aim of the present study was to evaluate the difference in "time to extubation" and "ICU length of stay" between the primary bolus doses of Pancuronium and Cisatracurium as the sole muscle-relaxing agent administered during the induction of anesthesia.

Methods

The research proposal for the present study was approved by the Ethics Committee of Shahid Rajaei Cardiovascular, Medical and Research Center, Tehran, Iran and the study was thereafter conducted over a twelve-month period in the center.
From all adult patients with coronary artery disease admitted to the cardiac operating room of the hospital for coronary artery bypass grafting, 110 cases were selected after a power analysis (power=0.80, beta=0.2, alpha=0.05) and were randomly divided into two groups of equal number. Case allocation was done using a closed box, containing 110 paper slips equally numbered one or two. Patients drawing out the number one slips were allocated to the Pancuronium group and those with the number two slips were placed in the Cisatracurium group for the induction of anesthesia.
Patients expected to have prolonged intubation and mechanical ventilation intervals (e.g. those with a diagnosis of aortic dissection, severe chronic pulmonary obstructive disease, any history of hypothyroidism, neuromuscular dysfunction, mononeuropathy or polyneuropathy, excessive bleeding in the postoperative period, and unusual arousal state in the postoperative period) as well as those with an unstable hemodynamic status or a history of readmission to the operating room to control postoperative bleeding were excluded from the present study.
Apart from the administration of Pancuronium and Cisatracurium for the induction and facilitation of the endotracheal intubation for Groups I and II, respectively, the method of anesthesia, including the anesthetic drugs and the intravenous solutions, and the method of surgery and cardiopulmonary bypass strategy were the same for both groups.
All the patients were monitored after having been positioned on the operating table, using an indwelling catheter for non-dominant radial artery cannulation, five-lead electrocardiography, and pulse oxymetry. Anesthesia was inducted using Etomidate (0.25mg/kg) plus intravenous doses of Sufentanil (0.6-0.8µg/kg), followed by an infusion dose of 2 µg/kg per hour. Depending on the group to which the patients were allocated, either Pancuronium (0.1 mg/kg) or Cisatracurium (0.15mg/kg) was administered to facilitate endotracheal intubation. A central venous line was inserted via a right jugular venous approach.
Anesthesia depth was maintained using a combination of Propofol infusion (50-100 µg/kg/min, Sufentanil, and inhalational Isoflurane to keep the level of anesthesia depth within the range of 40 to 60 according the bispectral index (BSI) for assessing the level of anesthesia.
Cardiopulmonary bypass was preceded by the administration of heparin (300 IU/Kg) through the central venous line, and bypass was conducted after an ACT level of 480 or more was achieved. The mean arterial blood pressure was

maintained between 50 to 80 mmHg, and hypothermia was induced until a core body temperature of 30°C was attained, which was monitored with a nasopharyngeal temperature probe.

The target vessels having been grafted, the patients were rewarmed and the weaning process was commenced until a nasopharyngeal temperature of 37°C was recorded. If necessary, a combination of low-dose epinephrine plus nitroglycerine was started through the central venous line to achieve a stable hemodynamic status. The length of time from the patients' arrival at the ICU until their extubation was recorded. After the termination of the surgical procedure, the patients were transferred to the ICU while intubated and mechanically ventilated. The patients were extubated if they fulfilled the extubation criteria, including being able to cough and protect the airway, hemodynamic stability and MAP ≥70 mmHg, no serious arrhythmias, appropriate ventilation status, acceptable chest radiography and arterial blood gas (pH≥7.35), maximal inspiratory pressure at least 25 cmH2O, no considerable chest tube drainage and minimal secretions, comfortable on T-piece or CPAP with respiratory rate ≤ 20 breaths/minute, being awake, full muscle force recovery, and full central nervous system orientation. The patients were thereafter transferred from the ICU to the post-ICU ward if they met the standard protocol of the hospital, comprised of the following criteria: acceptable hemodynamic status, termination of dependence on inotropic agents for having a stable hemodynamic status, and no residual complaint of pain scores equal to or greater than 3 of 10 on a numeric rating scale. The length of time from the patients' arrival at the ICU until their transfer to the post-ICU ward was recorded.

Neuromuscular monitoring was performed for all the patients, and all the measurements were made using the train-of-four (TOF) scores. Two electrodes were used; one of them was placed on the wrist at the level of the ulnar nerve and the other electrode was placed about 6 cm proximal to it. After the administration of the muscle relaxant, the ulnar nerve was stimulated every 20 seconds using a TOF supramaximal stimulation of 40mA. The first measurement (TOF 1) was done following the administration of the hypnotic, amnestic, and opioid agents but prior to the administration of the muscle relaxant agent; TOF 2 was measured after the administration of the hypnotic, amnestic, opioid, and muscle relaxant agents; TOF 3 was the measurement done just prior to the commencement of cardiopulmonary bypass; TOF 4 was concomitant with the hypothermic period of bypass (just before the start of rewarming); TOF 5 was done after weaning from bypass; and TOF 6 was measured at the end of the operation, just before transferring the patients from the operating room to the ICU. While the patients were monitored continuously with respect to the depth of anesthesia using the BIS, the BIS score was documented at six points. The first one (BIS 1) was done just before the induction of anesthesia; BIS 2 was measured just before tracheal intubation; and BIS 3 to BIS 6 were measured concurrently with the related TOF measurements (i.e. BIS 3 and TOF 3, BIS 4 and TOF 4, BIS 5 and TOF 5, and BIS 6 and TOF 6). Data entry and analysis were carried out using SPSS software (version 11.5). The Student *t*-test and the Chi square test were used for data analysis, and a value of P less than 0.05 was considered statistically significant.

Results

A total of 110 patients were allocated to two groups of 55 with no difference in terms of age, weight, cardiopulmonary bypass pump time, clamp time, operation time, the least temperature reached during the cooling period, and the preoperative ejection fraction values. However, "time to extubation at the ICU" and "postoperative ICU length of stay" were different between the two groups (Table I).

Table I. Distribution of the variables in the study; figures are demonstrated as mean ± standard deviation.

Variables	Pancuronium group	Cisatracurium group	P value
Age (years)	56.6±11.5	54.5±11.8	0.33
Weight (Kg)	69.6±12.5	70.1±9.1	0.8
CPB time (minutes) *	93.3±31	99.9±23.5	0.34
Aortic clamp time (minutes)	54.9±21.9	57.1±20.8	0.67

Operation time (minutes)	229.4±53.6	223.2±45.5	0.134
Least temperature (Centigrade) **	32.1±1.6	31.9±1.6	0.38
Preoperative EF ***	44.8±6.7	46.5±6	0.18
Time to extubation in ICU (minutes)	332±78	262±57	0.01
Time for post-op ICU stay (hours)	52.8±6.6	44.5±4.1	0.02

* CPB: Cardiopulmonary bypass ** The least temperature reached during the cooling period *** The preoperative ejection fraction values

The results of TOF monitoring, albeit not statistically different between TOF 1 and TOF 2, were statistically different for TOF 3 to TOF 6; these results were higher in the Cisatracurium group (Table II).

Table II. Train-of-Four results during the course of anesthesia

TOF number	Pancuronium group	Cisatracurium group	P value
TOF 1	99.2±5.4	100±0.0	0.32
TOF 2	2±14.1	0.4±2.8	0.43
TOF 3	3±12	26.3±27.4	0.00
TOF 4	7.7±15.1	66.1±25.5	0.00
TOF 5	39.4±24.5	87.6±21.7	0.00
TOF 6	67.6±28.3	92.9±22.5	0.00

TOF: Train-of-Four neuromuscular monitoring

A comparison of the depth of anesthesia monitoring results (i.e. before the induction of anesthesia and throughout the course of the surgery) between the two study groups demonstrated no statistically significant difference (Table III).

Table III. Bispectral index scores during the course of anesthesia

Bispectral index scores	Pancuronium group	Cisatracurium group	P value
BIS 1	91.9±3.4	90.9±3.7	0.16
BIS 2	49.6±7.1	49.8±6.1	0.86
BIS 3	46.9±4.4	48.5±9.3	0.26
BIS 4	47.3±5.7	48.2±7.6	0.48
BIS 5	48.7±5.3	49.8±7.2	0.4
BIS 6	48.1±4.8	50.3±8.6	0.11

BIS: Bispectral index scores

The results for the patients' diaphragmatic movements are demonstrated in Table IV.

Table IV. Diaphragmatic movements in the two groups

		Pancuronium group	Cisatracurium group	Total
Diaphragmatic movement status	no	52	39	91
	yes	3	16	19
	Total	55	55	110

P- value for chi square test= 0.001; (degree of freedom= 1)

There was a statistically significant difference between the two study groups with regard to the diaphragmatic movement status. Three patients in the Cisatracurium group and 2 patients in the Pancuronium group received extra doses of muscle relaxant agent at the surgeon's request. In total, 19 patients had diaphragmatic movements, for all of whom a first dose of sodium thiopental (2 mg/Kg) was administered, which resulted in only the aforementioned 5 patients requiring the extra muscle relaxants.

Conclusion

There was no difference between the Pancuronium and Cisatracurium groups in terms of the study variables except for "time to extubation at the ICU" and "postoperative ICU length of stay". With the muscle relaxants administered at the time of anesthesia induction without any further maintenance dose, the patients in the Cisatracurium group were extubated earlier and had a shorter ICU length of stay than those in the Pancuronium group.

Not all the similar studies conducted hitherto have reached similar results. In one study including 1,094 patients, no relationship was demonstrated between the use of shorter-acting opioid and neuromuscular blocking drugs and ICU length of stay after the extubation of the patients or even postoperative ICU length of stay.[3] In contrast, another study showed that ultra fast-track anesthesia afforded sufficient control of the hemodynamic status and consequently smoothed the progress of extubation in the operating room.[4] These divergent results may be in part begotten by the dissimilar effects of muscle relaxants and opioids and also the contribution of the confounders.

The results of the present study demonstrated that having an appropriate depth of anesthesia aids the administration of shorter-acting muscle relaxant agents (like Cisatracurium compared with Pancuronium) and thus confers earlier extubation and shorter ICU length of stay. These results were achieved when administering a single dose of muscle relaxants for intubation during anesthesia induction, with only a few patients requiring extra doses.

Conflict of Interest

No conflicts of interest have been claimed by the authors.

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