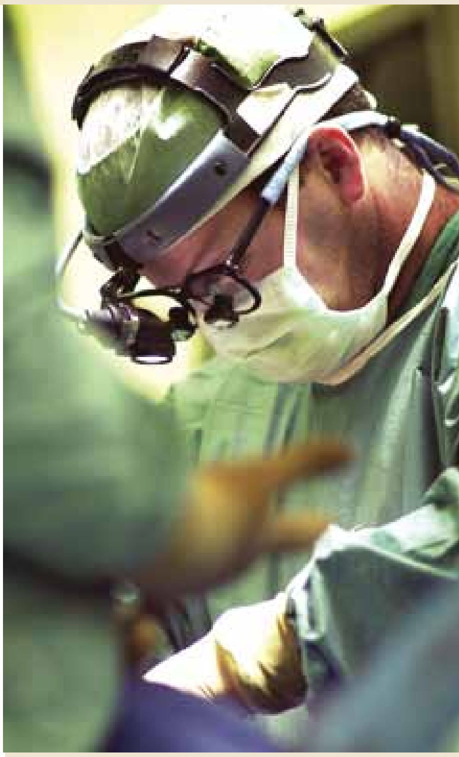
Assessing the Effect of Eliminating Maintenance Dose of Atracurium during Coronary Artery Bypass Graft Surgery



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Objective: Comparing the effect of using a single intubation dose of Atracurium to a single intubation dose plus a maintenance infusion dose during coronary artery bypass graft surgery

Methods and Main Results: 100 patients with a mean age of 55 ± 13.5 years (range 18 to 75 years undergoing elective Coronary Artery Bypass Graft surgery were evaluated in two different groups, group B(50 persons) used bolus dose of Atracurium and group M (50 persons) received the intubation plus Maintenance doses of Atracurium. Patients were compared by demographic, hemodynamic, probable diaphragmatic movement during the surgery, extubation time and ICU staying time. Mean systolic blood pressure had statistically significant differences between two groups; however, these differences seemed to be clinically unimportant. ICU stay was also significantly different between the two groups. It was observed that the mean time of surgery was shorter in "B" in than "M" group, which differed statistically significant that was not totally depending on anesthesiology management.

Conclusions: Atracurium bolus intubation dose could be used in cardiac surgery instead of maintenance infusion dose and it facilitates reduction of patients ICU staying and costs, but requires monitoring of the depth of anesthesia and neuromuscular blockade throughout the operation time to avoid patient movement and awareness.

Keywords: coronary artery bypass, fast track, airway extubation, cardiac bypass pump

ntroduction:

The intensive care unit (ICU) is an important component of the total cost of patient management after coronary artery bypass grafting (CABG). Because discharge from the ICU is impossible when the patient is intubated (1, 2), early extubation evolved as the main part of the fast-track method in cardiac anesthesia. (3, 4, 5) As long as we use a short-acting neuromuscular blocking agents we could have a normal neuromuscular transmission shortly after the end of surgery and we could accomplish a fast-track strategy this way. (6, 7, 8, 9) Administration of the maintenance infusion dose of neuromuscular blocker leads to an increase in paralysis time for the patients after the surgery. This is especially true after using a long-acting neuromuscular blocker such as Pancronium. (13, 14, 15, 20, 21) Hypothermia alters the distribution and decreases the metabolism of most drugs, including neuromuscular blockers. (18)

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Muscle strength is reduced during hypothermia, and it influences the detection of the twitch response. (25, 26) The impairment of metabolic function of the kidneys and liver during CPB as a result of hypoperfusion is expected to diminish the drug clearance rate. It also decreases acetylcholine concentration. Application of CPB causes an electrolyte shift, in particular, decreasing the plasma concentration of magnesium and calcium resulting in diminished muscle contractility. (20, 21) As the need for a neuromuscular blocker during hypothermic CPB is significantly reduced, continuous infusion of a neuromuscular blocker or frequent bolus administration might not be necessary. (10, 11, 12)

Residual paralysis in cardiac surgery is an important side effect in the postoperative period and an important reason for delayed extubation. (23, 27, 28) Now, in most centers, monitoring the depth of neuromuscular blockade is not used routinely; as a result, residual paralysis is not detected in the early postoperative period and these patients need sufficient sedation until normal neuromuscular blockade returns. This may take hours, delaying early extubation. (22)

The aim of this study is to compare the influence of a maintenance infusion dose of Atracurium to a single bolus intubation dose in early extubation, reducing the length of stay and attendant cost of the ICU.

Method:

The research proposal for the present study was approved by the Ethics Committee of Shahid Rajaei Heart Center, Tehran, Iran. The study was conducted over a four-month period. Participants were chosen from all adult patients admitted to the cardiac operating room of the hospital, 100 cases were selected after a power analysis (power=0.80, beta=0.2, alpha=0.05) and were randomly divided into groups of equal number. Case allocation was done using a closed box, containing 100 paper slips equally numbered one or two. Patients with the number one slips were allocated to the Bolus (B) Group and those with the number two slips were placed in the Maintenance (M) Group for the induction of anesthesia.

Table1- Distribution of the variables in the study

	Bolus Dose (n = 50)	Maintenance Dose (n = 50)	P value
Age (year)	54 ± 11.8	55 ± 15	0.871
Female/Male	18/32	26/24	0.107
Weight (kg)	70 ± 9.1	69 ± 12.7	0.752
Renal Diseases	2 (4%)	2 (4%)	> 0.99
Respiratory Diseases	1 (2%)	1 (2%)	> 0.99
Hypertension	29 (58%)	27 (54%)	0.534
Diabetes	12 (24%)	15 (30%)	0.499
Beta Blockers	24 (48%)	32 (64%)	0.107
Calcium Channel Blockers	7 (14%)	6 (12%)	0.766
Statins	24 (48%)	28 (56%)	0.423

Exclusion criteria:

Patients who were expected to have left ventricular ejection fraction of less than 30%, renal insufficiency (creatinine > 2 mg/dL), severe liver disease (alanine aminotransferase and/or aspartate aminotransferase >75 IU/dL), severe chronic pulmonary obstructive disease, any history of hypothyroidism, neuromuscular dysfunction, mononeuropathy or polyneuropathy, were excluded from the present study.

IAll the patients were monitored after having been positioned on the operating table, using an indwelling catheter for non-dominant radial artery cannulation, 5-lead electrocardiography, and pulse oxymetry. Anesthesia was inducted using Etomidate (0.25mg/kg) or Thiopental (304mg/kg) plus intravenous doses of Sufentanil (0.6-0.8μg/kg), followed by an infusion dose of 2 μg/kg per hour and Midazolam (1 μg/kg). Depending on the group to which the patients were allocated, either bolus intubation dose of Atracurium (0.5mg/kg) B group, or intubation plus maintenance infusion M group (6micro/kg/min) was administered. A central venous line was preferably inserted via a right jugular or subclavian venous approach. Anesthesia depth was maintained using a combination of Midazolam, Sufentanil, and inhalational Isoflurane within the range of 40 to 60 according to the bispectral index (BSI) for assessing the level of anesthesia. Cardiopulmonary bypass was preceded by the administration of heparin (300 -400 IU/Kg) through the central venous line, and bypass was conducted after an ACT level of 480 or more had been achieved. The mean arterial blood pressure was maintained between 50 to 80 mmHg, and hypothermia was induced until a core body temperature of 34°C had been attained. Body temperature was monitored with a nasopharyngeal temperature probe. The target vessels having been grafted, the patients were re-warmed and the weaning process was commenced until a nasopharyngeal temperature of 36-37°C had been 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, which included hemodynamic stability, appropriate ventilation status, minimal chest tube drainage, 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. Transfer criteria included: acceptable hemodynamic status, termination of dependence on inotropic agents to maintain a stable hemodynamic status, and no residual complaint of pain scores equal to or greater than 3 of 10 on a numeric rating scale.

Table 2-Distribution of variables throughout the surgery and after

	Bolus Dose (n = 50)	Maintenance Dose (n = 50)	P value
Pre pump Systolic Blood Pressure (mmHg)	140 ± 20.6	149 ± 17.1	0.015
Pre pump Diastolic Blood Pressure (mmHg)	79 ± 10.6	82 ± 11.5	0.265
Pre pump Heart Rate (beat/min)	82 ± 14	84 ± 12	0.522
TOF	4.1 ± 1.1	4.5 ± 1.0	0.124
Pump Time (min)	100 ± 23.5	94 ± 40.1	0.377
Clamp Time (min)	57 ± 20.8	52 ± 25.9	0.277
Operation Time (min)	253 ± 41.5	282 ± 62.6	0.008
Extubation Time (hours)	8 ± 2.8	8.6 ± 1.5	0.171
ICU stay (hours)	47.5 ± 4.4	49.5 ± 2.6	0.012

Table3-Comparison of patients and diaphragmatic movement during the surgery

	Bolus Dose (n = 50)	Maintenance Dose (n = 50)	P value
Patients' Movement	15 (30%)	0	< 0.001
Diaphragmatic Movement	7 (14%)	1 (2%)	0.027
BULUS NEED	32 (64%)	1 (2%)	< 0.001
MR.NEED	5 (10%)	0	0.050

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. 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 re-warming); 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 score. The BIS score was documented at 6 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). Student's t-test and the Chi square test were used for data analysis.

If a patient had a BIS value more than the goal range (45-55) or showed diaphragmatic movements, we increased the dose of hypnotic maintenance dose to reach the target BIS. If this approach was not sufficient, we administered one bolus of neuromuscular blocker (0.1mg/kg).

Results:

One-hundred patients (50 in each group) with a mean age of 55 ± 13.5 years (range 18 to 75 years) with no difference in terms of age, weight, cardiopulmonary bypass pump time, clamp time, the least temperature reached during the cooling period, and the preoperative ejection fraction values, were enrolled. Surgery type was elective coronary artery bypass graft. Mean systolic blood pressure had statistically significant differences between the two groups, but these differences seemed to be clinically unimportant.

We found "postoperative ICU lengths of stay" were different between the two groups (p=0.012) (Table 1). It was observed that the mean time of surgery was 253 ± 41.5 minutes in "B" and 282 ± 62.6 minutes in "M" group, which though statistically significant (p value = 0.008), was not definitely dependent on anesthesia management . Postoperative residual paralysis was reduced in group B but was not statically important. Fifteen patients in B group had movement during the operation but only one in M group showed movements. ($P<0.001$) Diaphragmatic movement was also observed in 7 patients in B group and 1 in M group. This difference was statically noticeable. ($P=0.027$)

Discussion:

There have been advancements in cardiac surgery over the last two decades; the face of cardiac anesthesia has also changed. The concept of fast-track anesthesia demands the use of a short-acting neuromuscular blocker and the immediate re-establishment of normal neuromuscular transmission at the end of surgery. (10, 12) The patient should not be extubated postoperatively as long as they do not have normal neuromuscular transmission (23, 27). Although it seems obvious that fast track reduces the total cost of treatment of CABG patients in different ways, ICU care is still an important component of post CABG care, and earlier transfer to the surgical ward would decrease the costs of hospitalization. (1, 2, 3)

This study is a double-blind prospective randomized clinical trial. We compared the effects of bolus and bolus plus infusion of a maintenance dose of Atracurium in patients undergoing elective CABG surgery. The patients were not different in demographics, comorbidities or drug consumption. The type of surgery was also the same in both groups. Results showed that the hemodynamics in B group was statically different from M group; the heart rate and diastolic pressure weren't statically different, but systolic pressure statically was lower in B group. However, the difference was not clinically important. Anesthesia duration (from induction till ICU arrival) in B group was statically lower than M group and it was not completely dependent on anesthesia management.

The extubation time was not significantly different in both groups. The ICU length of stay was statistically shorter in the B group from M group, indicating the earlier normalization of neuromuscular transmission in B group.

Paralysis time was not different in both groups, and it didn't appear the same as previous studies. Diaphragmatic movement apparently was greater in B group.

Overall, it showed that the bolus dose of Atracurium leads to surgical field difficulty due to patient movement, diaphragmatic movement and the incremental hypnotic maintenance dose requirements.

HOWEVER the postoperative paralysis time would be decreased and fast-track recovery would be achieved sooner and ICU length of stay would be reduced. It is recommended that if fast-track recovery is a goal, monitoring the neuromuscular blockade and depth of anesthesia, a bolus intubation dose of Atracurium would be preferable. However, a maintenance dose of Atracurium would result in less of a surgical field problem and create an easier task for the anesthesiologist.

Appendix:

The following criteria were adapted from Murphy et al 19

Criteria for Weaning Mechanical Ventilatory Support

- Hemodynamic stability
- Absence of uncontrolled arrhythmias
- Central temperature greater than 36.0°C
- Chest tube drainage less than 100 ml in the past 2 h
- Arterial oxygen tension greater than 60 mmHg with an oxygen fraction less than 0.5
- pH greater than 7.3 Criteria for Tracheal Extubation
- All of the criteria for weaning ventilatory support met
- Negative inspiratory force greater than _20 cm H20
- Patient responsive to simple commands

Criteria for Intensive Care Unit Discharge

- Patient alert and cooperative
- No inotropic support
- No significant arrhythmias
- Arterial oxygen saturation greater than 90% with inspired oxygen fraction less than 0.5
- Chest tube drainage less than 50 ml in the past 2 h
- No seizure activity
- Urine output greater than 0.5 ml • kg_1 • ml_1

Criteria for Hospital Discharge

- Hemodynamically stable
- Stable cardiac rhythm
- Noninfected incisions and absence of elevated temperatures
- Patient is able to void and have bowel movements
- Independent ambulation and feeding

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