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Anesthesia in Adult Cardiac Surgery without Maintenance of Muscle Relaxants: A Randomized Clinical Trial

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Abstract: There may be no need for muscle paralysis during cardiac surgery when adequate anesthesia is provided. We studied intra- and post-operative conditions during cardiac surgery without maintenance muscle relaxant therapy. Eighty adult patients who were candidates for elective coronary artery bypass graft surgery were randomly allocated into two groups. In the noMR or study group (noMR group; n = 40) only an intubation dose of cisatracurium (0.15 mg kg^{-1}) was administrated, as opposed to the control group (MR group; n = 40), who had a continuous infusion added to the intubation dose. The anesthesia level was maintained at a Bispectral score of 40-50 using a propofol infusion. A remifentanil infusion was titrated to control patient hemodynamic response. During surgery, any minor (fine body or respiratory muscle movements) or major (coarse body movements or bucking/caught) movements were recorded. Postoperatively, analgesia was provided by remifentanil. The surgical condition was classified into three states: good (no movement), acceptable (minor movements), or poor (major movements). Anesthesia, surgery and postoperative characteristics were compared between the two groups. Statistical analysis was performed in only 78 patients (noMR = 38, MR = 40). The demographic and preoperative characteristics of the two groups were comparable. Intra-operative propofol consumption was the same, but significantly more remifentanil was used in the noMR group (p = 0.001). Post-operative characteristics and complication rates did not differ between the two groups. There were no movements in the MR group patients, while in the noMR group one patient had major movement and three had minor movements. We concluded that omitting maintenance muscle relaxants in adult cardiac surgery or eliminating residual muscle paralysis at the end of the surgery without improving early outcome can increase patient intra-operative movement risk.

Key words: Neuromuscular blocking drugs, residual muscle paralysis, cisatracurium, coronary artery bypass graft surgery, fast-track cardiac surgery

INTRODUCTION

The main aim of a fast-track cardiac surgery program, mainly early tracheal extubation within the first 6-8 h, is reducing pre-and post-operative (Post-Op) hospital stays and costs. Fast-track cardiac surgery requires coordinated and multidisciplinary action on the part of the heath care team. Anesthetic maneuvers are important components of fast track surgery. Unlike delayed extubation, early tracheal extubation can reduce complications, hospital stay time and costs without increasing cardiopulmonary complications, mortality and sympathoadrenal stress (Cheng *et al*., 1996a; Vricella *et al*., 2000; Murphy *et al*., 2002a; Berg *et al*., 1997; Reis *et al*., 2002; Myles *et al*., 2003; Wong *et al*., 1999; Guller *et al*., 2004; Watanabe *et al*., 2004; Cheng *et al*., 1996b). Neuromuscular blocking drugs are commonly used in cardiac surgery. Different levels of neuromuscular blockade are needed for various operations or during different stages of a single operation (Mogensen, 2005). Deep neuromuscular blockade is usually used during cardiac surgery and monitoring or reversal of the neuromuscular blockade is not done routinely. Thus, residual muscle paralysis at the end of surgery is very common (Maybauer *et al*., 2007; Ouattara *et al*., 2001; Murphy *et al*., 2003; Naguib *et al*., 2007). This paralysis

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can increase Post-Op mechanical ventilation time and delay tracheal extubation. Thus, omitting residual muscle paralysis at the end of surgery may be helpful in fast track surgery. A few studies and authors have recently stated that if an adequate level of anesthesia is provided, there is no need for continuous paralysis during the entire cardiac surgery (Cammu, 2004; Gueret *et al*., 2004). Gueret *et al*. (2004) managed anesthetic care of cardiac surgeries with only a single intubation dose of atracurium or cisatracurium without any adverse impact on the surgery. However, their study did not have a comparative control group. We hypothesized that a comparative study may be more reliable in determining whether omitting residual muscle paralysis at the end of the cardiac surgery can help early tracheal extubation and reduce ICU or postoperative hospital stay times. Thus, we conducted a randomized clinical trial of patients who were candidates for elective on-pump coronary artery bypass graft surgery (CABG). In the study group we omitted routine maintenance muscle relaxant administration, while in the control group we maintained a continuous infusion of cisatracurium during surgery. We compared anesthesia, surgical and Post-Op characteristics between the two groups.

MATERIALS AND METHODS

After approval from the our local institutional ethics committee and written preoperative informed consent from all patients, eighty adult patients who were candidates for elective on-pump CABG in a university hospital (Madani Heart Center, Tabriz-Iran) in an 11-month period from December 2007 to November 2008 were studied prospectively. Patients were randomly divided into either the study or control groups. In the study group, named the noMR group (n = 40), only an intubation dose of cisatracurium was administrated. In the control group, named the MR group (n = 40), an additional continuous infusion of the cisatracurium was added to the same initial intubation dose. Exclusion criteria were patients with ejection fraction (EF) = 30%, recent acute myocardial infarction or unstable angina, NYHA functional class = III, renal, hepatic, psychologic and neurologic diseases, opioid addiction, ASA class = IV and patients older than 75 years old. All surgeons were blind to the purpose of the study throughout the entire study. Oral diazepam (10 mg) was administered to the patient the night before surgery and approximately 1 h before the patient's transfer to the operating theater. An IM morphine sulfate 0.1 mg kg^{-1} plus promethazine 0.5 mg kg^{-1} was administrated as premedication. All patients were admitted to the operating theater in the early morning. An anesthetic nurse prepared the treatment drug in a 50 mL syringe: pure 0.9% NaCl or saline containing 40 mg cisatracurium besylate (Nimbex, Glaxo Wellcome S.pA., Parma, Italy) for the noMR and MR groups, respectively.

After peripheral venous and arterial catheterization (right radial artery), a Peripheral Nerve Stimulator (PNS) (Mogensen, 2005; Gueret *et al*., 2004) and bispectral analyzer (BIS, Aspect 2000 EEG monitor and BIS sensor) electrodes were connected to the patient according to manufacturer's instructions (Aspect Medical Systems, 2006). The PNS electrodes were placed over the left ulnar nerve at the wrist and the accelerometer was fixed to the distal phalanx of the thumb. Anesthesia was induced with a 1-1.5 mg kg^{-1} bolus of propofol and remifentanil infusion. Remifentanil was initially infused at a rate of 1 μg/kg/min for a 2 min period and then 0.5 μg/kg/min for an additional 5 min. As soon as the patient had lost consciousness, PNS (TOF Watch SX®, Organon Ltd., Dublin, Ireland) was calibrated with a 50-mA output in Train Of Four (TOF) mode according to the factory instructions. After cisatracurium administration (0.15 mg kg^{-1} in 15-20 sec), the TOF count was measured every 15 sec and when the TOF count reached zero, the trachea was intubated. Propofol was titrated to produce a constant BIS level of 40-50 during surgery. After tracheal intubation, remifentanil infusion was continued at a rate of 0.1-0.5 μg/kg/min to maintain a Mean Arterial Blood Pressure (MABP) of about 0-30% lower than the preinduction value or between 60 to 80 mmHg during cardiopulmonary bypass (CPB). When the arterial blood pressure could not be controlled with remifentanil adjustment, nitroglycerin or phenylepherine infusion was used. The neuromuscular blockade level was measured as a TOF ratio/count every 15 min in all patients. When neuromuscular blockade recovered to a TOF count of 3, the treatment drug infusion was started at the 0.1 mL/kg/h (equal to 1.3 μg/kg/min of the cisatracurium in the control group). In the control (MR) group, the TOF count was kept at 1-3 by adjusting of the treatment drug infusion rate. An anesthesiologist (first anesthesiologist) who was blinded to the treatment drug and TOF results throughout surgery was responsible for any anesthesia and cardiopulmonary bypass management of the patient except adjustment of the treatment drug. The TOF ratio/count measurement and treatment drug adjustment was performed by a second anesthesiologist. The second anesthesiologist was blind to the treatment condition until it could be discovered as he was controlling twitch response. Only the second anesthesiologist could see or read the TOF results. Invasive monitoring of the arterial and central venous blood pressure, BIS, 5 lead ECG, pulse oximetry, end tidal capnography, nasopharyngeal and palm temperature and arterial blood gas analysis were performed as routine practice. Nasopharyngeal

temperature was maintained above 36.0°C using a heat exchanger blanket or CPB machine throughout anesthesia. During surgery any minor or major movement by the patient were noted and recorded by the first anesthesiologist. Any fine face, extremity, or diaphragmatic contractions without any adverse impact on surgery were considered minor movements. Major movements had an adverse impact on the surgical condition and were defined as any coarse extremity or body movements, diaphragmatic contractions such as bucking and any surgical complaints related to the lack of relaxation. If any major movements occurred, bolus doses of IV cisatracurium (2 mg) were administrated by the first anesthesiologist. All surgeries were performed via a conventional median sternotomy. Approximately 15 min before skin closure, a bolus dose of the fentanyl at 3 μg kg^{-1} was administrated. At the end of the surgery, propofol and the treatment drug infusion were discontinued. Infusion of remifentanil was continued as an analgesic. At the end of the surgery, the surgical condition was classified and recorded by the first anesthesiologist in three states as good (no movement), acceptable (minor movements), or poor (major movements). In the ICU, invasive hemodynamic, ECG and temperature monitoring, pulse oximetry and arterial blood gas analysis (every hour) were done. Remifentanil infusion was continued until patients could get out of bed or after 24 h. The IV Fentanyl at 1 μg kg^{-1} was administrated if further analgesia was needed. Neuromuscular blockade was monitored immediately after ICU admission and then every 15 min until the TOF ratio reached 0.9. Patients were warmed and shivering was managed with IV 2 mg midazolam and/or 30 mg meperidine. All ICU staff were blind to the purpose of the study and TOF results. Mechanical Ventilation (MV) was set up in the SIMV mode and a weaning process was performed as routine activity by the ICU staff. The local protocol criteria for weaning off of mechanical ventilation include stable hemodynamic conditions with minimal inotropic or vasodilator support, neurologically stable with a consciousness level score of 2 on the Ramsay Sedation Scale (Table 1) (Ramsay *et al*., 1974), an inspired oxygen fraction≤0.5 resulting in a PaO_2>70 mmHg, pH>7.3, a bleeding rate = 50 mL h^{-1} for at least 2 h and a core temperature≥36.5°C. The tracheal tube was removed when both PEEP and pressure supports were≤5 cmH_2O (MacIntyre, 2001; Price and Rizk, 1999). When the patient could get out of bed, remifentanil infusion was discontinued and a PRN IM bolus morphine sulfate was used as analgesic. Follow-up of patients was continued until hospital discharge and any complications were discovered and recorded.

Table 1: Ramsay sedation scale

Response	Score
Anxious, agitated, restless	1
Awake, cooperative, oriented, tranquil	2
Semi-asleep but responds to commands	3
Asleep but responds briskly to glabellar tap or loud auditory stimulus	4
Asleep with sluggish or decreased response to glabellar tap or loud auditory stimulus	5
No. response can be elicited	6

SPSS (version 11.5, SPSS Inc., Chicago, IL, USA) software was used for statistical analyses. Normal distribution of continuous data were tested by the Kolmogorov-Smirnov test. Pearson's Chi-squared and Mann-Whitney's tests were applied to compare categorical variables or continuous variables that did not meet normal distribution. An independent sample t-test was used to compare normally distributed continuous variables between the two groups and one-way repeated measure ANOVA was used to compare continuous variables in each group. Statistical analyses were performed with a confidence interval of 95% and were considered two-tailed. Data differences were considered statistically significant when the p≤0.05.

RESULTS

Two patients refused to participate in the study before anesthesia induction. Statistical analysis was performed for the remaining 78 patients (study or noMR group, n = 38; control or MR, n = 40). Generally there were no significant differences between the two groups in demographic characteristics. However numbers of diseased coronary arteries was high in study group but left ventricle ejection fraction was low comparing to control group (Table 2). Heart rate and mean arterial blood pressure at various times were comparable between the two groups.

Table 2: Demographic and preoperative characteristics of the two groups

Characteristics	*noMR(n = 38)	†MR(n = 40)	p value
Male/Female	23/15	25/15	1.000
Age	57.6±9.5	57.3±8.8	0.893
Weight	69.8±11.9	74.6±13.4	0.102
Height	161.0±9.6	164.2±8.1	0.110
ASA Functional class II/III	8/30	13/27	0.312
Numbers of diseased coronary artery	2.37±0.59	2.70±0.56	0.013‡
DM	5 (13.2%)	7 (18.4%)	0.756
Cigarette smoking	14 (38.9%)	20 (52.6%)	0.263
HTN	26 (68.4%)	29 (76.3%)	0.805
HLP	21 (55.3%)	24 (63.2%)	0.819
LM lesion	3	5	0.712
LVEF (%)	46.5±7.1	50.1±6.7	0.021‡
Basic heart rate	77.3±13.5	78.7±17.9	0.696
Basic MABP	92.8±15.6	95.0±12.3	0.488

*Patients who did not receive maintenance cisatracurium during anesthesia maintenance, †Patients who received maintenance cisatracurium during anesthesia maintenance, DM: Diabetes mellitus; HTN: Hypertension; HLP: Hyperlipidemia; LM lesion: Left main coronary artery lesion; LVEF: Left ventricular ejection fraction; MABP: Mean arterial blood pressure. ‡Different between two groups. Data are Mean±SD or No. (percent)

Table 3: Intra-operative characteristics of the two groups

Intra-opretive Characteristics	*noMR(n = 38)	†MR(n = 40)	p value
Inotrope used during operation	10 (26.3%)	8 (20.0%)	0.595
‡Nitroglycerine used during operation	9 (15.8%)	14 (35.0%)	0.326
Anesthesia time (minute)	311.6± 61.0	329.7±58.2	0.182
Surgical time (minute)	2617 ±71.2	283.4±53.9	0.132
§CPB time (minute)	99.2±18.9	105.4±30.9	0.289
Propofol consumption (μg/kg/min)	76.8±20.3	68.4± 22.9	0.096
Remifentanil consumption (μg/kg/min)	0.44 ± 0.17	0.26±0.13	0.000
Surgical status good/acceptable/poor	34/3/1	40/0/0	0.109
¥ Time to TOF ratio≥ 0.9 in OR (min)	92.29±28.01	-----	

*Patients who did not receive cisatracurium during anesthesia maintenance, †: Patients who received cisatracurium during anesthesia maintenance, ‡: Infusion rate > 0.1 mg/kg/min, § Cardiopulmonary bypass, ¶: Different between two groups, ¥ TOF: Train of four, OR: operation room. Values are Mean±SD or No. (percent)

Anesthesia, CPB and surgical times were comparable between the two groups (Table 3). The need for vasodilators or inotropic agents were not different between the two groups. Although, propofol consumption was the same in the two groups, intraoperative remifentanil usage was significantly higher in the noMR group than in the MR group (p = 0.001). The surgical condition in all patients in the MR group was good, but in the noMR group only 34 patients had a good surgical condition. In three patients, the surgical condition was acceptable (minor movements such as fine face and extremity movements) and one patient had major movements in the late CPB and post-CPB period (vigorous extremity movements, bucking and cough along with the surgical complaints related to the lack of the relaxation). Major movements were easily controlled with 2 mg IV cisatracurium. The time to obtain a TOF ratio of = 0.9 in the noMR patients was 92.29±28.01 min (Table 3) and all patients had a TOF ratio = 0.9 at ICU admission (Table 4). All of the patients in the MR group had a TOF count = 4 when they were admitted to the ICU (3.1±0.92) and 144.32±96.88 min was needed to obtain a TOF ratio of 0.9 (Table 4).

The need for inotropic agents and a vasodilator in the ICU was comparable in the two groups. There were no differences in the two groups in sedation, mechanical ventilation/tracheal extubation times, time needed to get out of bed, time to leaving the ICU and Post-Op hospital stay times (Table 4). All patients had a TOF ratio = 0.9 when they were extubated.

Due to hemodynamic instability and its dependence on a high dose of inotropic support, three patients were transferred to the ICU with an unclosed sternum (one patient in noMR and two in the MR group). One patient from the noMR group who was transferred to the ICU with an unclosed sternum died in the 6th h of ICU admission because of heart failure.The two other patients had their sternum closed uneventfully on the day after surgery. One patient in the MR group complained of intra-operative recall. We could not find any explanation for this since BIS was maintained in an acceptable narrow limit using propofol infusion. Another patient (from the noMR group) had a brief episode of tonic-clonic seizure that was controlled with 2 mg midazolam with an intact neurologic outcome. He had a previously diagnosed calcified ascending aorta in the echocardiographic report as well as in surgical report when punching the aorta for proximal graft anastomosis during surgery. Hemodynamic complications were comparable (Table 5). Only one patient (from the noMR group) required early reintubation 6 h after early tracheal

Table 4: Post-op characteristics of the two groups

Post-op Characteristics	*noMR(n = 38)	†MR(n = 40)	p value
‡TOF in ICU admission	0.98±0.06 (TOF ratio)	3.1±0. 92 (TOF count)	
Time to obtain a TOF ratio≥ 0.9 in ICU (min)	0	144.32±96.88	
Inotrope used in ICU	15 (39.4%)	10 (25.0%)	0.226
§ Nitroglycerine used in ICU	14 (45.2%)	13 (34.2%)	0.813
Sedation time (hour)	4.3±2.9	3.7±3.1	0.395
Mechanical time/ extubation time (hour)	8.3±5.9	7.4±5.3	0.497
Out of bed time (hour)	24.2±8.7	23.4±6.4	0.648
ICU stay time (hour)	62.7±30.3	64.5±25.6	0.776
Postoperative hospital stay time (day)	7.1±3.3	8.1±4.3	0.246

*Patients who did not receive cisatracurium during anesthesia maintenance, †: Patients who received cisatracurium during anesthesia maintenance, ‡: TOF: train of four, § Infusion rate>0.1 μg/kg/min. Values are Mean±SD or No. (percent)

Table 5: Postoperative complications of the two groups

Complications	*noMR (n = 38)	†MR (n = 40)	p value
Neuropsychologic			
Psychosis/hallucination	2	3	1.000
Recall	0	1	1.000
Agitation	2	1	0.610
Seizure	1	0	0.487
Cardiovascular			
Unclosed sternum	1	2	1.000
Postoperative atrial fibrillation	4	5	1.000
Bleeding	3	2	0.671
Reoperation	2	1	0.610
Hypotension	3	4	1.000
Post-Op myocardial infarction	4	2	0.425
Intra-aortic balloon pump	2	2	1.000
Respiratory			
Tracheal reintubation	1	0	0.487
Emphysema	0	1	1.000
Chilothorax	1	0	0.487
Long intubation>0 h (%)	7 (18%)	6 (15%)	0.767
Others			
Mortality	1	0	0.487
Readmission to ICU	1	1	1.000
Shivering	7	1	1.000
Nausea and vomiting	3	3	0.671

*Patients who did not receive cisatracurium during anesthesia maintenance, †: Patients who received cisatracurium during anesthesia maintenance

extubation because of hypotension and postoperative myocardial infarction. The need for long intubation (more than 10 h) was comparable. Shivering was the most common complication, but there were no significant differences between the two groups. There were no infectious complications.

DISCUSSION

The main uses of neuromuscular blocking drugs in cardiac surgery are to facilitate tracheal intubation, optimize the surgical condition, reduce oxygen consumption and prevent hypothermia-induced shivering. An ideal neuromuscular blocking drug used in fast-track cardiac surgery needs to produce a stable cardiovascular status and also have a short onset time, short clinical duration, the ability to provide sufficiently profound neuromuscular blockade during surgery and a short recovery time, with or without reversal (Hemmerling *et al*., 2008). After the onset time, the most important characteristic for these drugs is a short and predictable recovery time, preferably independent of hepatic or renal function. During cardiac surgery, many anesthetists primarily focus on hemodynamic management and put less emphasis on the residual paralysis at the end of the surgery. Thus, residual muscle paralysis is very common after cardiac surgery and can delay tracheal extubation.

The choice of neuromuscular blocking drug (Cammu *et al*., 2002; McEwin *et al*., 1997; Naguib *et al*., 2007) and its repetitive or continuous administration (Cammu *et al*., 2005; Mirinejad *et al*., 2007) during surgery affects the rate of residual muscle paralysis at the end of surgery. In 2002 a national postal survey in the USA showed that pancuronium is the most common neuromuscular blocking drug used during cardiac surgery (Murphy *et al*., 2002b). Even if pancuronium is administrated as a single-dose during induction of anesthesia, residual muscle paralysis is very common (McEwin *et al*., 1997; Van Oldenbeek *et al*., 1999; Murphy *et al*., 2003; Thomas *et al*., 2003). Although, replacing long-acting muscle relaxants with intermediate-acting drugs has decreased residual muscle paralysis at the end of surgery, It is still not uncommon after continuous infusion or repetitive administrations of intermediate-acting muscle relaxants (Hayes *et al*., 2001).

Traditionally, deep muscle relaxation is used during cardiac surgery and monitoring or reversing the residual neuromuscular blockade at the end of surgery is not routinely done. Thus, postoperative residual muscle paralysis is very common (Maybauer *et al*., 2007; Ouattara *et al*., 2001; Murphy *et al*., 2003; Naguib *et al*., 2007) and can increase postoperative mechanical ventilation time and delay tracheal extubation. In the hope of reducing residual muscle paralysis, several authors have recently recommended that along with providing an adequate level of anesthesia, it is possible to omit neuromuscular blockade from cardiac surgery (Cammu, 2007; Gueret *et al*., 2004; Metz, 2003). Gueret *et al*. (2004) with only a single intubation dose of atracurium or cisatracurium. They did not report any intra-operative movement or adverse impacts on the surgery, but the lack of a control group in their study made their postoperative outcome results unclear. In a comparative study, Cammu *et al*. (2007) did not see any movement or increase in anesthetic requirement (propofol and remifentanil) when they omitted maintenance muscle relaxant administration. We studied both surgical conditions and early outcomes. We observed a good condition in only 34 of 38 patients who had no maintenance muscle relaxant administration. One patient had vigorous movements (body and respiratory) and three others had fine movements relatively late in the operative period. Although, vigorous movements were easily controlled, such sudden and unpredictable movements may adversely affect surgery. On the other hand, although at admission to the ICU there was no residual muscle paralysis in the noMR group, there was not any improvement in the early Post-Op outcome and in the need for Post-Op mechanical ventilation/tracheal tube. In addition, the complication rate did not decrease significantly. Cammu *et al*. (2007) reported the same finding about extubation time, ICU and hospital stay and complication rate. This may suggest that several hours of residual muscle paralysis after cardiac surgery does not have an adverse impact on patient outcome. It may not always be a safe anesthetic practice to provide a suitable surgical condition with a deep level of anesthesia alone (Stansky and Shafer, 2005; Monk *et al*., 2005; Weldon *et al*., 2002). Very deep anesthesia may increase the infection rate and compromise patient hemodynamics. We kept patients from both groups in a relatively deep level of anesthesia and we therefore cannot present any comparative conclusions about the effects of deep anesthesia on outcome. However, it must be remembered that a deep level of anesthesia can counteract the beneficial effects of omitted residual muscle paralysis at the end of surgery, especially in patients with a compromised cardiovascular status. Although several studies claim that neuromuscular blocking drugs have minimum anesthetics effects (Liu *et al*., 2005; Forbes *et al*., 1979), the general agreement is that neuromuscular blocking drugs do not have any significant anesthetic effect (Vasella *et al*., 2005; Fahey *et al*., 1989; Greif *et al*., 2002; Dahaba *et al*., 2004;

Chan and Fanzca, 2006). Thus, it is recommended that anesthesiologists avoid using unnecessary muscle paralysis when possible. We adjusted the dose of propofol to provide an equal BIS score (40-50) in both groups. Considering that the same dose of propofol was needed in both groups, we believe that neuromuscular blocking drugs don't have any anesthetic properties. Cammu *et al.* (2007) reported using the same doses of propofol and remifentanil in their study. We therefore must provide an explanation for the different findings in our study, since we saw more remifentanil consumption in the noMR group. Although, there is not enough evidence about BIS reliability as an indicator of the anesthetic level (Scarlett *et al.*, 2005), it is still clinically useful. The reliability of the BIS index is strongly influenced by the anesthetic technique (Kissin, 2000). Opioids have a minimal effect on the BIS score compared to hypnotic agents such as propofol. When propofol is used as the primary anesthetic, there is a strong, inverse relationship between the BIS index and the probability of a movement response to pain. When opioids are used as the main component of the anesthesia, the correlation between the BIS index and patient movement becomes less significant (Sebel *et al.*, 1997). As an explanation for the greater remifentanil consumption in the noMR group, two theories can be considered. First, it is possible that by controlling patient hemodynamics in the noMR group, we kept our patients in a deeper level of anesthesia by remifentanil, which was not reflected in the BIS score. In the study by Cammu *et al.* (2007), it was not clearly defined if or when any vasodilator was used in cases where the hemodynamics could not be kept within the predefined limits with remifentanil alone. In other words, the requirement for anesthetic may be increased in the absence of neuromuscular blocking drugs, which was reflected in the remifentanil consumption, but Cammu may have covered it (increased anesthetic requirement) by administrating more vasodilator. Another theory is that, considering the electromyographic activity interference with the BIS processing (a high BIS score in the absence of neuromuscular blocking drugs) (Chan and Fanzca, 2006; Renna *et al.*, 2002; Vivien *et al.*, 2003; Bonhomme and Hans, 2007; Messner *et al.*, 2003), the noMR group patients may have been under a deeper level of anesthesia. However, if this was the case, it is expected that instead of remifentanil, more propofol would have been used in the noMR group. Again, it may be concluded that the anesthetic requirement was increased in the absence of neuromuscular blocking drugs (more remifentanil was used but it was not reflected in the BIS score). In addition, in the study by Cammu *et al.* (2007), the anesthetic requirement (propofol) also increased, although this effect was not significant ($p = 0.07$). Although, they interpreted this finding as the interference effect of the electromyographic activity on the BIS processing algorithm, it may really be due to an increased anesthetic requirement that was not significant because of the small sample size or methodological problems.

In summary, we found that omitting maintenance neuromuscular blockade after an initial intubation dose of cisatracurium, thus eliminating residual muscle paralysis at end of cardiac surgery, does not reduce complications or improve early Post-Op outcome. In addition, this may predispose patients to vigorous intra-operative movements that have an adverse impact on the surgery. Considering a patient's preoperative health and physical status and the surgical procedure is probably the most powerful predicting factor for Post-Op sedation and mechanical ventilation needs, delayed tracheal extubation, complication rate and increased ICU or hospital stay period (Hemmerling *et al.*, 2008; Cheng, 1998). Early tracheal extubation after a major surgery in patients with a compromised preoperative cardiovascular status may predispose them to numerous problems such as hypoxemia, hypercapnia, atelectasia and hemodynamic instability.

Finally, we must address the limitations of our study: difference in numbers of diseased coronary arteries and left ventricular ejection fraction between two groups, a small sample size, magnesium sulfate administration before the aorta declamping in purpose to decrease arrhythmias (that can affect muscle relaxant pharmacodynamic) and possible unidentified oral commands by surgeons to continue sedation. All of these factors may alter the collected data accuracy or results.

CONCLUSION

In summary, we found that omitting maintenance neuromuscular blockade (residual muscle paralysis at end of cardiac surgery) after an initial intubation dose may cause patients to undergo vigorous intra-operative movements without markedly improving their Post-Op outcome.

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