Neuromuscular Block during Beating Heart Surgery, Comparison between Pancuronium, Rocuronium, and Cisatracurium

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ABSTRACT

Background: The use of long acting muscle relaxants e.g. pancuronium in fast-track cardiac surgical patients may be associated with delays in clinical recovery, and this can be avoided by using other short acting muscle relaxants e.g. rocuronium, or cisatracurium.

Aim: to study the different haemodynamics and neuromuscular effects of pancuronium, rocuronium, and cisatracurium,and to evaluate the incidence and severity of residual neuromuscular blockade in patients undergoing beating heart coronary artey bypass surgery.

Methods: Sixty patients, ASA physical status III–IV, aged 38–60 yr, with single vessel, or two or three vessel disease, scheduled for beating heart coronary artery bypass grafting and an expected time of surgery between 2.5-3.5hr were included***.*** All patients received a standardized fentanyl / sevoflurane anesthesia. For intraoperative muscle relaxation, patients were randomized into three groups (n=20):

I : ***Group P:*** Received pancuronium (0.08-0.1 mg/kg)

II : ***Group R:*** Received rocuronium (0.6-0.8 mg/kg).

III : ***Group C:*** Received cisatracurium(0.15-0.2 mg/kg).

Haemodynamic measurements were repeated after induction of anesthesia but before muscle relaxants (baseline), then 2, 5, and 10 minutes after drug injection.In the intensive care unit, train-of-four (TOF) ratios were measured each hour until weaning off ventilatory support was initiated. Neuromuscular blockade was not reversed in all patients. Thirty minutes after tracheal extubation, patients were examined for signs and symptoms of residual paresis.

Results: There were no clinically significant differences between the three groups as regards demographic characteristics, and haemodynamic data. Nearly complete recovery of neuromuscular function occurred within 3 hours of ICU admission in the rocuronium group (TOF ratio: 0.93 ±0.06), and cisatracurium group (TOF ratio: 0.91 ±0.05),

whereas significant residual neuromuscular block was present at 3 hours in the pancuronium group (TOF ratio: 0.26 ± 0.27) ($P < 0.05$). Patients in the rocuronium and cisatracurium groups were more likely to be free of signs and symptoms of residual paresis than patients in the pancuronium group.

Conclusions: It was concluded that the use of intermediate-acting relaxants muscle relaxants may be associated with improvements in neuromuscular recovery and fewer signs and symptoms of muscle weakness in the fast-track, off pump cardiac surgical patient.

Key words: Beating heart surgery, Neuromuscular block, Pancuronium, Rocuronium, Cisatracurium.

Introduction:

Coronary artery bypass graft (CABG) surgery without cardiopulmonary bypass (Off pump) is gaining popularity [1].One of the advantages of this technique is the fast recovery, and early extubation, with subsequent early ambulation, and short stay in intensive care unite (ICU), and fast discharge of the patient from the hospital, the so called (fast-track cardiac surgery).

There are many factors should be considered for choice of neuromuscular blocking drugs (NMBDs) in coronary artery disease patients undergoing beating heart coronary artery bypass surgery. The heamodynamic effects, the onset and duration of action, and the metabolism of the drug should be the most important factors to be considered[2].

The primary aim of fast-track cardiac anesthesia is to facilitate tracheal extubation within 1-8 h of intensive care unit (ICU) admission[3].

For safe and reliable achievement of fast recovery after cardiac surgery, full recovery from the residual effects of opioids, benzodiazepines, and NMBDs should be present before tracheal extubation is accomplished. Therefore, some authors advocate the use of shorter-acting NMBDs in the fast-track cardiac patient[4-5].

In patients undergoing cardiopulmonary bypass (CPB), the use of pancuronium has been associated with prolonged neuromuscular blockade and delays in tracheal extubation[5].

Following beating heart surgery, it is expected that the use of long-acting NMBDs e.g. pancuronium may be associated with prolonged postoperative recovery when compared with the use of shorter-acting relaxants e.g rocuronium, cisatracurium [6].

Rocuronium is a nondepolarizing muscle relaxant of intermediate duration that differs from its analogue, vecuronium, by having a rapid onset of action. The onset time of rocuronium is shorter than that of vecuronium and approaches that of succinylcholine, making it a useful component of a rapid sequence induction of anaesthesia. Rocuronium has a duration of action that is similar to that of vecuronium, demonstrates little or no cumulative effect, and is only minimally influenced by the type of anaesthetic technique. Furthermore, the cardiovascular stability of rocuronium has been demonstrated by observing no changes in heart rate and blood pressure in response to doses of up to 0.9 mg/kg[7].

Cisatracurium is a neuromuscular blocker for which the safety, efficacy, pharmacokinetics, and pharmacodynamics have been demonstrated in ASA physical status I and II patients up to and including 8 x ED95 doses. Low doses of cisatracurium (2 x ED95) had minimal haemodynamic effects in patients with coronary artery disease[8].

Aim of the work:

The aim of this clinical study was to investigate the haemodynamic effects, and the time course of recovery of neuromuscular function after beating heart surgery in patients randomized to receive either pancuronium, rocuronium, or cisatracurium.

The aim also was to test the hypothesis that the use of the shorter acting NMBDs rocuronium or cisatracurium in the operating room (OR) would result in less clinically significant neuromuscular blockade in the ICU, and fewer signs and symptoms of residual paresis in the fast-track patient than would the use of the long-acting NMBD pancuronium.

Materials and Methods:

The study was performed at Soliman Fakeeh Hospital and approved by the Hospital Ethics Committee and informed consent was obtained from each patient.

Patients:

Sixty male and female patients whose age between 38-60yrs, and body weight
between 65–100 kg, with single vessel, or two or three vessel disease, scheduled for beating heart coronary artery bypass grafting and an expected time of surgery between 2.5- 3.5hrs
were ***included.***

Exclusion criteria: Patients who had a history of cardiac surgery, severe congestive heart failure,or had a history of drug abuse, neuromuscular disorder or malignant hyperthermia, or had a history of renal , respiratory, hepatic or psychiatric disease were excluded.

Methods:

All patients received a standard premedication consisting of 1-3mg lorazepam, plus 150mg zantac orally on the evening of surgery .

Prior to induction of anesthesia, pulse-oxymetry, ECG leads II and V_2 were continuously recorded. Peripheral intravenous lines, radial artery catheter, and pulmonary artery catheter (Becton Dickinson; Criticath ^{TM} SP 5107HTD) were placed using local anesthesia.Pulmonary artery catheters were positioned for thermodilution readings of cardiac output (HP Component Monitoring system M1094A, Hewlett Packard, Palo Alto, CA).

Anesthesia was induced using propofol 0.5-1.5 mg/kg then, 3-5 µg/kg fentanyl was given in 5 min. During fentanyl infusion, ventilation was assisted manually with 100% oxygen supplemented with sevoflurane.

After induction of anesthesia, and before administration of muscle relaxation, all baseline haemodynamic measurements were taken after a 5-min stabilization period. This haemodynamic measurements included heart rate (HR), mean arterial pressure (MAP), central venous pressure (CVP), mean pulmonary arterial pressure (MPAP), pulmonary capillary wedge pressure (PCWP), cardiac output (CO), cardiac index (CI), systemic vascular resistance (SVR), and pulmonary vascular resistance (PVR).

For intraoperative muscle relaxation, patients were randomized into three groups (n=20). The randomization assignment was concealed in an envelope until the patient entered the OR.

The three groups were as follow:

I : ***Group P:*** Received pancuronium(0.08-0.1 mg/kg),
(Alpax, HIKMA pharmaceuticals,Amman-Jordan)

II: ***Group R:*** Received rocuronium (0.6-0.8 mg/kg),
(Esmerone, (Organon,Dublin, Ireland)

III: ***Group C:*** Received cisatracurium(0.15-0.2 mg/kg),
(Nimbex, Glaxo-Smith-Kline,S.P.A, Parma, Italy).

Following baseline measurements, the NMBD was administered as an intravenous bolus into a central vein over 5–10 sec, according to group assignment. All haemodynamic measurements were repeated 2, 5, and 10 minutes after drug injection. After these three measurements, endotracheal intubation was attempted.

After intubation, anesthesia was maintained with a continuous infusion of fentanyl
(3 µg/kg/h), propofol infusion 4-6 mg/kg/h and oxygen air mixture (40%—60%), with supplementary sevoflurane as needed. Controlled mechanical ventilation was adjusted to maintain end-tidal carbon dioxide between 34 and 40 mmHg.

Intra-operative monitoring of neuromuscular transmission:

Additional maintenance dosing of NMBDs was determined on the basis of peripheral nerve stimulation of the facial nerve carefully to reduce the risk of NMBD overdosage. The facial nerve was stimulated using the train-of-four (TOF) -nerve stimulator *(MultiStim,VARIO-PAJUNK®- Germany),* and the response at the muscles surrounding the eye was observed. One or two responses to TOFstimulation were maintained throughout the intraoperative period. 20% of the initial dose of muscle relaxant was provided as a bolus to achieve this goal. No NMBDs were administered during the last 30 min in the OR.

Increases in blood pressure or heart rate were treated by increasing the sevoflurane concentration or with 50-150 µg of fentanyl, up to a total dose of 15 µg/kg, in the OR. Nitroglycerin or nitroprusside infusions were started if these measures were unsuccessful. Hypotension was treated with phenylephrine, or volume replacement, as indicated.

Before the end of operation and during sternal closure, propofol sedation was initiated in the form of propofol infusion between 25-75µg/kg/min, and it was maintained during transfer to the ICU and during the period of controlled mechanical ventilation.

Post-operative monitoring of neuromuscular transmission:

In the ICU, monitoring of neuromuscular transmission was performed using TOF test. The ulnar nerve at the wrist was supramaximally stimulated (50 mA), 0.2 msec square wave stimuli (frequency of 2 Hz for 2 sec) every ten seconds TOF, and the responses at the adductor pollicis were recorded using the *TOF-Watch*

acceleromyograph(Organon,Dublin, Ireland). The acceleromyographic probe was placed on the distal portion of the thumb, which was allowed to move freely.

The fade ratios (The ratio of the fourth twitch (T4) to the first twitch (T1), is defined as the ratio of the amplitude of (T4) relative to that of (T1) in a TOF stimulus) were recorded each 30 minutes for three houres until weaning off ventilatory support was initiated. The mean of three consecutive TOF fade ratios was used for each evaluation.

All monitoring was conducted according to guidelines established for good clinical research practice in pharmacodynamic studies of neuromuscular transmission which included:

Core temperatures were maintained >35°C and hand temperatures at >32°C by using warmed blankets, the study arm was immobilized on an arm board, which was positioned parallel to the patients' body [9]**.** All TOF data were collected by an investigator blinded to group assignment. Neuromuscular blockade was not reversed because the administration of anticholinesterase drugs in the ICU may eliminate the differences between the groups.

At the start of ventilatory weaning when the ptient fulfill the criteria for weaning from mechanical ventilatory support, propofol infusions were turned off or the rate of the infusions was significantly reduced to allow the patient to awaken.

The time required to wean from ventilatory support (from the initiation of reduced mechanical ventilation until tracheal extubation) as well as the duration of mechanical ventilation were noted.

Standard care was applied for all patients , and weaning from ventilatory support and tracheal extubation was accomplished when strictly defined criteria were met. ICU staffs involved in the care of study patients were blinded to group assignment.

Criteria for weaning mechanical ventilatory support (adapted from ***Cheng et al***. [10]***):***

Hemodynamic stability
Absence of uncontrolled arrhythmias
Central temperature >36.0°C
Chest tube drainage <100 mL in the past 2 h
Arterial oxygen tension >60 mm Hg with an oxygen fraction <0.5 with pH >7.3

Criteria for tracheal extubation:

All of the criteria for weaning ventilatory support met
Negative inspiratory force more than -20 cm H2O
Patient responsive to simple commands.

Thirty minutes after tracheal extubation, patients were examined for signs and symptoms of residual paresis. Standardized examinations were conducted by a single investigator to reduce intraobserver variability. A brief physical examination was conducted to detect signs of residual paresis:

Patients were asked to maintain a 5-sec head-lift and then a 5-sec leg-lift. These tests were not performed against resistance.

After this, subjects were directed to hold a wooden tongue depressor between their incisor teeth. They were asked to resist removal of the tongue depressor as gentle pressure was applied by the examiner. Patients were allowed one opportunity to pass or fail each test.

After these tests, subjects were directly asked by the investigator about the presence or absence of the following symptoms:

-visual symptoms (difficulty focusing eyes),

-symptoms of facial weakness (difficulty smiling),

-symptoms of oral and pharyngeal muscle weakness (difficulty in smiling or swallowing),

and symptoms of generalized muscle weakness.

Questions were presented to the subjects in an identical order and manner.

Also, the patient outcome, lengths of ICU stay and hospital stays were evaluated.

Statistical Analysis:

The results are reported as mean values ± standard deviations (SD). Nominal data were compared between the three groups by using Fisher's exact probability test.Haemodynamics, and TOF data were analyzed with repeated-measures analysis of variance (ANOVA) to compare changes within each group and paired Student's t-test to compare different group data. Significance was $P < 0.05$.

Results:

As regards the demographic characteristics ,there were no differences in the mean age, height, or weight of patients, sex distribution, ASA physical status, concomitant diseases or medications, number and type of the grafts, duration of surgery and anesthesia among the three groups as seen in Table (1).

In all patients, there were no clinically important haemodynamic changes before intubation as seen in Table (2), and [Figure 1 :(1-8)].

Table (1): Demographic data of all groups (mean ± SD):

Parameter	***Group P*** (n=20)	***Group R*** (n=20)	***Group C*** (n=20)
Age (yr)	46.3±8.3	48.2±6.7	47.5±8.1
Weight(kg)	79.2±11	77.5±7.6	78.4±9.3
Height(cm)	174±9	170±12	172±11
Male/female	16/4	15/5	14/6
ASA class III/IV	15/5	16/4	17/3
Ejection fraction	53±4	52±5	54±2
Previous MI	15	11	13
Previous CHF	3	2	4
Hypertension	17	16	18
Diabetes	10	11	13
History of smoking	9	10	8
Number of grafts	2.2±1	2.3±1	2.1±1
Duration of surgery (min)	175±24	181±19	172±26
Duration of anesthesia (min)	255±28	261±31	252±25

No significant difference between the three groups. P= Pancuronium,. R= Rocuronium,. C= Cisatracurium,
MI = myocardial infarction; CHF = congestive heart failure.

Table (2): Haemodynamic changes after injection of the muscle relaxant in all groups (mean±SD).

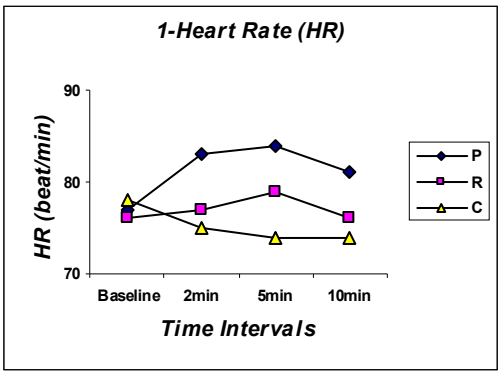
Parameter	***Baseline after induction***	***(2 min) after drug injection***	***(5 min) after drug injection***	***(10 min) after drug injection***

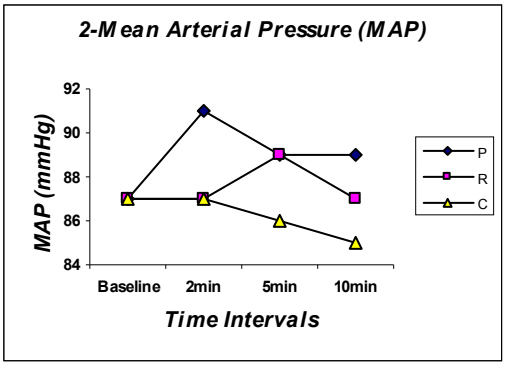
HR(bpm)				
Pancuronium	**74±7**	**79±8**	**81±6**	**78±5**
Rocuronium	**72±8**	**74±5**	**75±8**	**73±6**
Cisatracurium	**75±5**	**73±4**	**72±5**	**72±4**
MAP(mmHg)				
Pancuronium	**82±9**	**87±8**	**87±5**	**85±9**
Rocuronium	**84±7**	**85±5**	**86±7**	**84±6**
Cisatracurium	**83±8**	**82±9**	**82±8**	**83±5**
CVP(mmHg)				
Pancuronium	**11±3**	**10±4**	**10±2**	**10±3**
Rocuronium	**10±2**	**9±6**	**9±7**	**9±5**
Cisatracurium	**10±6**	**9±5**	**9±6**	**9±7**
MPAP(mmHg)				
Pancuronium	**19±3**	**20±4**	**19±5**	**19±4**
Rocuronium	**19±4**	**18±5**	**18±4**	**18±2**
Cisatracurium	**20±2**	**18±3**	**18±2**	**18±5**
PCWP(mmHg)				
Pancuronium	**11±3**	**10±3**	**10±2**	**10±1**
Rocuronium	**11±2**	**10±5**	**10±4**	**11±2**
Cisatracurium	**11±1**	**10±6**	**10±3**	**10±2**
CI(l/min/m^2)				
Pancuronium	**2.6±0.1**	**2.6±0.4**	**2.6±0.3**	**2.6±0.2**
Rocuronium	**2.4±0.3**	**2.4±0.4**	**2.4±0.5**	**2.4±0.6**
Cisatracurium	**2.5 ±0.2**	**2.4 ±0.7**	**2.4 ±0.8**	**2.5 ±0.1**
SVR(dyn.s.cm^{-5})				
Pancuronium	**2248±253**	**2252±224**	**2250±271**	**2251±234**
Rocuronium	**2273±236**	**2261±217**	**2265±228**	**2270±242**
Cisatracurium	**2251±261**	**2248±253**	**2248±253**	**2248±253**
PVR(dyn.s.cm^{-5})				
Pancuronium	**246±32**	**241±53**	**244±25**	**248±28**
Rocuronium	**278±27**	**257±36**	**258±23**	**257±38**
Cisatracurium	**252±31**	**218±62**	**222±53**	**220±25**

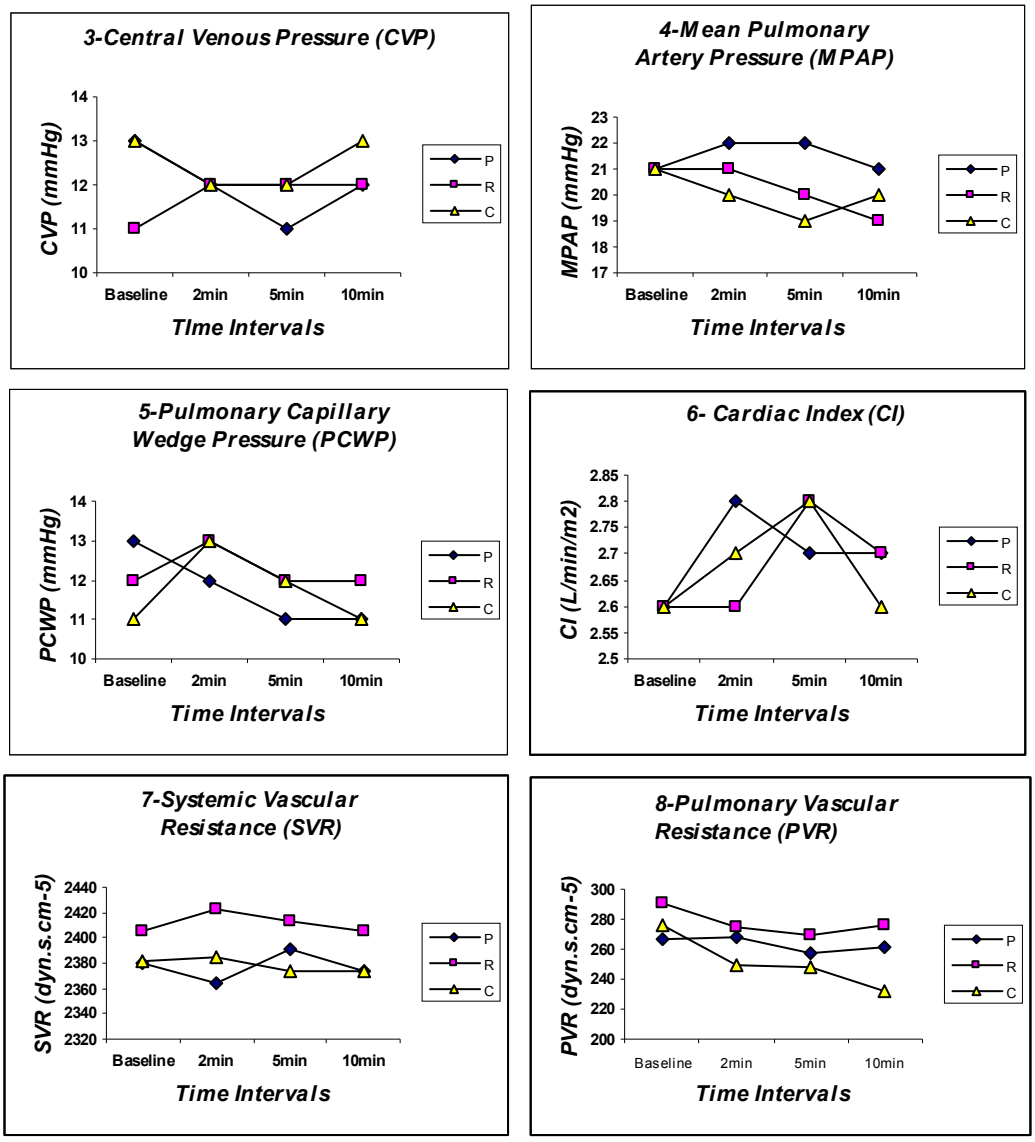
No significant difference between the three groups. HR=heart rate, MAP=mean arterial pressure,

CVP=central venous pressure, MPAP=mean pulmonary artery pressure, PCWP=pulmonary capillary wedge

pressure, CI=cardiac index, SVR=systemic vascular resistance, PVR=pulmonary vascular resistance.







[Figure 1 :(1-8)] Haemodynamic changes of all groups before intubation
P= Pancuronium,. R= Rocuronium,. C= Cisatracurium.
No clinically significant difference between the three groups.

Data of intraoperative drugs and fluid therapy are presented in Table(3).

Table (3): Intraoperative drugs and fluid therapy in all groups (mean ± SD):

Variable	***Group P*** (n=20)	***Group R*** (n=20)	***Group C*** (n=20)
Anesthetic Drugs:			
Total fentanyl (µg/kg)	12.8 ± 4.6	13.0 ± 2.9	12.9 ± 5.1
Muscle relaxant (mg/kg)	0.1 ± 0.02	2.08 ± 0.7	0.6 ± 0.08
Intraoperative fluid therapy:			
Crystalloids (ml)	570 ± 320	610 ± 260	590 ± 190
HES (ml)	1165 ± 95	980 ± 215	1050 ± 110
Intraoperative Urine output	420 ± 270	510 ± 190	490 ± 180

(ml) :			

No significant difference between the three groups.
P= Pancuronium,. R= Rocuronium,. C= Cisatracurium, HES= hydroxyethyl starch.

It is noted that in the pancuronium group only single dose of muscle relaxant was enough to cover the intraoperative period, while in the other two groups two or three additional maintenance doses (20% of the initial dose of muscle relaxant) were used.

In the ICU, as regards neuromuscular monitoring , TOF fade ratios are presented in [Figure 2].

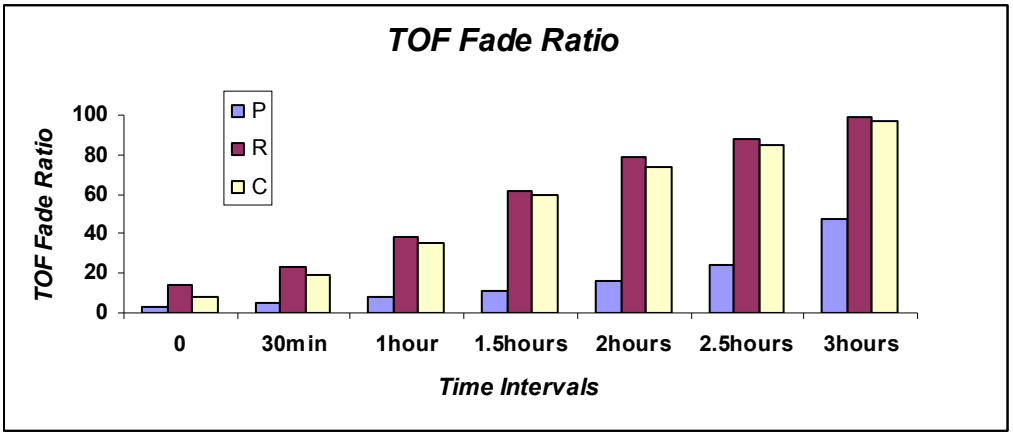


Figure 2. Train-of-four (TOP) fade ratios measured on arrival to the intensive care unit (Hour 0) and then each 30 minutes for the next 3hours. P= Pancuronium,. R= Rocuronium,. C= Cisatracurium Significant differences (P < 0.05) were noted between the rocuronium, cisatracurium and pancuronium groups at all measurement times,but no significant differences between rocuronium, and cisatracurium. Also, significant differences (P < 0.05) were noted between measurements at all times and those at Hour 0 within the rocuronium and cisatracurium groups,. and between measurements at 1.5, 2, 2.5, and 3hours and those at Hour 0 within the pancuronium group.

Nearly complete recovery of neuromuscular function occurred within 3 hours of ICU admission in the rocuronium group (TOF ratio: 0.93 ±0.06), and cisatracurium group
(TOF ratio: 0.91 ±0.05), whereas significant residual neuromuscular block was present at 3 hours in the pancuronium group (TOF ratio: 0.26 ± 0.27) ($P < 0.05$).

When weaning of ventilatory support was initiated in the rocuronium and cisatracurium groups, TOF ratios >0.8 were measured in all subjects. In contrast, only 2 of 20 patients in the pancuronium group had TOF ratios >0.8 at the start of the weaning process.

Times required to wean from mechanical ventilation were significantly less in the rocuronium group (76.9 ± 15.1 min) and in cisatracurium group (82.9 ± 16.3 min), than in the pancuronium group (102.6 ± 28.4 min) ($P < 0.05$).

Also, total durations of tracheal intubations, and durations of ICU stay were observed to be significantly less in patients who received rocuronium or cisatracurium when compared with those who received pancuronium ($P < 0.05$). Table (4).

Table (4): Postoperative mechanical ventilation, ICU stay, and hospital stay in all groups (mean ± SD):

Variable	***Group P*** (n=20)	***Group R*** (n=20)	***Group C*** (n=20)
Duration of ventilatory weaning (min)	102.6 ± 28.4	76.9 ± 15.1*	82.9 ± 16.3*
Duration of postoperative ventilation (hr)	5.3±0.4	2.8±0.6*	2.9±0.7*
Duration of ICU stay (days)	3±1	2±1*	2±1*
Duration of hospital stay (days)	8±2	7±3	7±3

**** Significantly lower than pancuronium group (P < 0.05).***
P= Pancuronium,. R= Rocuronium,. C= Cisatracurium.

No patients in the study developed airway obstruction or required reintubation.

Subjects who received pancuronium in the OR noted more signs and symptoms of residual muscle weakness in the ICU ($P < 0.05$). Table (5).

Table (5): Signs and symptoms of residual muscular weakness in the ICU (30 minutes after extubation) in all groups (mean ± SD):

Variable	***Group P*** (n=20)	***Group R*** (n=20)	***Group C*** (n=20)
Generalized weakness	12*	5	5
Unable to perform head-lift (5 s)	20*	2	3
Unable to perform leg-lift (5 s)	10*	2	2
Unable to resist removal of tongue depressor from between incisor teeth	9*	0	0
Difficulty focusing eyes	16*	1	1
Difficulty speaking	13*	4	5
Difficulty smiling	15*	2	2

**** Significantly higher than rocuronium and cisatracurium groups (P < 0.05).***
P= Pancuronium,. R= Rocuronium,. C= Cisatracurium.

Discussion:

Residual paralysis can result in serious morbidity due to inadequate ventilation, hypoxia, hypercarbia, acidosis, and the need for reintubation and mechanical ventilation, all factors that delay discharge from the (ICU) and that subject patients to significant risk[6].

In open heart surgery using cardiopulmonary bypass (CPB), their were many studies have examined the adequacy of neuromuscular recovery in the early postoperative period[3-6].

MeEwin etal. 1997 [4] measured TOF fade ratios in cardiac patients on arrival to the ICU and again 30 minutes later. Thirty minutes after ICU admission, all patients in the pancuronium group had TOF ratios <0.7, compared with 3 of 10 patients in the rocuronium group.

Van Oldenbeek et al. 1999 [5] measured TOF ratios in the ICU in cardiac surgical patients who received pancuronium as the sole NMBD. When criteria for discontinuation of sedation and extubation were met, the median TOF ratio was 0.23.

Murphy et al. 2003[3] measured TOF fade ratios in cardiac patients on arrival to the ICU and 60 min intervals until weaning off ventilatory support was initiated. A mean TOF ratio of 0.99 was measured in the rocuronium group 4 hours after admission to the ICU. This represents nearly complete recovery from the effects of muscle relaxants administered in the OR. In the pancuronium group, a mean TOF ratio of only 0.26 was observed 4 hours after ICU arrival. Significant residual paresis (TOF ratios <0.7) was present in some of the patients in the pancuronium group for more than 8-10 hours in the ICU. A significantly larger number of patients in the pancuronium group (32 of 39) noted at least one symptom of muscle weakness when compared with the rocuronium group (7 of 40).

The aim of this clinical study was to investigate the haemodynamic effects, and the time course of recovery of neuromuscular function after beating heart surgery in patients randomized to receive either pancuronium, rocuronium, or cisatracurium.

As regards haemodynamic effects of the three drugs , in this study, all patients demonstrated statistically and clinically non significant changes in HR, MAP, MPAP, CVP and PCWP from preinjection over the 10-min postinjection period.The changes from control were minimal for the three drugs and these results are consistent with the findings of ***Reich et al.*** [8] and many others , who concluded that patients undergoing anaesthesia for cardiovascular surgery are inherently unstable and do show some degree of haemodynamic variability over time in the absence of surgical stimulation. The changes seen in the current study are typical of the anaesthetized unstimulated patient, and have been seen in other studies of similar design.

Cisatracurium and rocuronium generally lack cardiovascular side-effects during high-dose opioid anaesthesia and thus have advantages for use during CABG procedures [11].

Both rocuronium and cisatracurium are characterized by an intermediate duration of action. Cisatracurium is four to five times more potent than rocuronium. Rocuronium had a faster onset of action, a shorter clinical duration, and a faster spontaneous recovery rate compared with equipotent doses of cisatracurium[12].

In this study, only a single dose of pancuronium (0.08-0.1 mg/kg) was enough to cover the intraoperative period in pancuronium group (a moderate level of neuromuscular blockade (one or two twitches) was maintained during the intraoperative period), while in the other two groups two or three additional maintenance doses (20% of the initial dose of muscle relaxant) were used. However, the clinical duration of action was shorter for rocuronium (30-35 min) than that for an equi-effective dose of cisatracurium (40- 45 min).The clinical durations of action of rocuronium and cisatracurium, reflect those values described in the literature for these muscle relaxants when they are given during balanced anaesthesia both with and without volatile drugs[12].

Times required to wean from mechanical ventilation and total durations of tracheal intubations were significantly less in the rocuronium and cisatracurium group than in the pancuronium group; and this results were consistent with the findings of ***MeEwin etal.*** [4] ,
Van Oldenbeek et al. [5] , and ***Murphy et al.*** [3] with the difference that all times were lower than times in that studies because these three studies were in cardiac surgical cases using CPB.

Off pump coronary artery bypass procedures are usually of shorter duration, and patients undergoing this procedures are expected to recover and ambulate faster than in cases using CPB.

Alterations in the pharmacokinetic and pharmacodynamic properties of pancuronium, which are induced by CPB, can contribute to postoperative residual muscle weakness[13]. Increased sensitivity of muscles to pancuronium has been shown to persist into the post-CPB period[14].

Also, drug elimination may be reduced by relative hypo-perfusion of the liver and kidney or by hypothermia during CPB. This is true for cisatracurium and for rocuronium. Moreover, as the clearance of cisatracurium, one of the stereoisomers of atracurium, is highly dependent on Hofmann degradation, temperature and pH changes associated with CPB are likely to affect its pharmacokinetics more than those of other neuromuscular blocking drugs[13].

As regards signs and symptoms of residual muscle weakness, the results of this study were in accordance with the findings of the previous studies that examined residual muscle paralysis following cardiac surgery[3-5]. On physical examination, the most common symptoms were a sensation of generalized weakness, difficulties in speaking, and visual disturbances. Many patients in the pancuronium group also noted weakness in the muscles of facial expression and difficulties in smiling.

Kopman et al. 1997 [15]concluded that the most sensitive test for residual paresis may be the ability to maintain incisor teeth apposition; TOF ratios must exceed 0.85 before subjects can resist a vigorous effort to remove a tongue depressor.

In this study, TOF ratios was not measured when patients were examined for signs and symptoms of residual paralysis, because supramaximal nerve stimulation is painful in awake patients . However, it was very clear that all signs and symptoms of residual muscle weakness were significantly high in pancuronium group ($P < 0.05$). Table (5).

Because patients in rocuronium and cisatracurium groups were early extubated and
showed minimal residual muscle weakness, they were ambulated earlier, with subsequent shorter ICU stay than patients in the pancuronium group($P < 0.05$). Table (4).

The short-acting muscle relaxants are more titratable, are easier to use, and are associated with a wider margin of safety than the long-acting relaxants, and problems during recovery are less frequent because of the more rapid clearance of the relaxant[16].

Under ideal circumstances, and with the use of anticholinesterase drugs in the ICU,
long-acting relaxants may be equally good, but their successful use requires experience and a certain level of predictability in the surgery[16].

It was concluded that the use of intermediate-acting relaxants muscle relaxants may be associated with improvements in neuromuscular recovery and

fewer signs and symptoms of muscle weakness in the fast-track, off pump cardiac surgical patient. To reduce the risk of residual neuromuscular blockade in this cases , it is recommended to use the intermediate-acting NMBDs, with routine examinations for clinical signs of muscle weakness, and pharmacological reversal of residual neuromuscular block whenever pancuronium is used.

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