

Research Article

Rocuronium vs Vecuronium: A comparison of Intubating condition, hemodynamic parameters and post-operative outcome in patients of coronary artery bypass graft surgery

Himanshu Shah^{*1}, Mrugank Bhavsar¹, Rama Upadhyaya¹, Hetal Rathod¹, Jaishree S. B.²
and Mansi Gandhi¹

¹SBKS Medical Institute and Research Centre, Sumandeep Vidyapeeth, Vadodara, Gujarat, India

²GCS Medical College, Hospital and Research Centre, Ahmedabad-380 025. Gujarat, India

*** Correspondence Info:**

Dr. Himanshu Shah,

Associate Professor, Consultant Cardiac Anesthetist

SBKS Medical Institute and Research Centre, Sumandeep Vidyapeeth, Vadodara, Gujarat, India

Email address: ha99090@gmail.com

Abstract

Background: To compare Intubating condition, hemodynamic parameters and post operative outcome between Rocuronium as an Intubating agent followed by Atracurium as a maintenance and Vecuronium as Intubating and maintenance agent.

Material and Methods: 50 patients posted for elective Off Pump CABG were divided into two groups. They were premedicated with Inj. Glycopyrrolate 5mcg/kg and Inj. Ondansetron 0.1 mg/kg. They were all preoxygenated with 100% O₂ for 5 minutes. All patients were induced with Inj. Fentanyl 5mcg/kg and Inj. Midazolam 0.15 mg/kg IV. Group RA (n=25) patients were induced with Inj. Rocuronium 1mg/kg and in Group VV (n=25) were induced with Inj. Vecuronium 0.2mg/kg. They were all maintained with O₂, Air, Isoflurane (0.2-0.6%), In RA group, anesthesia maintenance include infusion of Atracurium 0.5mg/kg/hr, Fentanyl 2mcg/kg/hr and Midazolam 5mcg/kg/hr. In VV group, Anesthesia was maintained by Intermittant bolus doses of Vecuronium 0.02 mg/kg, Fentanyl 2mcg/kg and Midazolam 0.02 mg/kg every hour.

Observation and Results: Patients were monitored for Intubating condition/ time of onset of muscle relaxant, hemodynamic parameters such as HR, MAP, SPO₂, SVO₂, PVR, PAP, SV, CO. Patients were observed for BIS and Neuromuscular monitoring (Train of Four). Intraoperative fluid and blood requirement, urine output and need of Inhalational agent requirement were compared.

Extubation time, complications, length of ICU stay and cost were compared.

Rocuronium has less time of onset with hemodynamic stability. In Group RA, hemodynamic stability was well maintained throughout the surgery, extubation time and complication rate were significantly lower than group VV.

Conclusion: Rocuronium was superior as Intubating agent. Combined use of Rocuronium followed by Atracurium provided more hemodynamic stability intraoperatively with better postoperative outcome.

Keywords: Rocuronium, Vecuronium, Atracurium, Coronary artery bypass graft surgery

1. Introduction

Cardiac surgery is defined as the surgery on the heart or great vessels to correct Ischemic heart disease, valvular defects or congenital defects. Along with advancement in cardiac surgery, cardiac anesthesia has also entered into the "Fast Track" cardiac anesthesia. "Fast-track anesthesia" demands the use of non depolarizing neuromuscular blocking drugs with short duration of action, combining the ability to provide (if necessary) sufficiently profound neuromuscular blockade

during surgery and immediate re-establishment of normal neuromuscular transmission at the end of surgery. Residual neuromuscular paralysis is still considered as the prime issue along with early extubation and prolongs length of ICU stay as well.¹

Cardiovascular stability is of utmost great importance with an ideal neuromuscular blocker. Vecuronium and Atracurium have been introduced earlier with intermediate duration of action. Previously Vecuronium was reported to be the best in terms of hemodynamic stability but recent reports suggest that Vecuronium causes severe bradycardia especially with high dose fentanyl anesthesia. Atracurium has been proven to cause histamine release. In addition, both of these have relatively slower onset of action.²

Rocuronium is a new aminosteroidal competitive muscle relaxant. Studies in human confirmed that onset of action is to be rapid in comparison with Vecuronium as well. Combination of two neuromuscular blockers has never been tried previously in cardiac surgery.^{2,3}

Our aim is to compare Intubating condition, hemodynamic parameters and post-operative outcome in Rocuronium followed by Atracurium, in comparison with Vecuronium alone in patients posted for elective coronary artery bypass grafting surgery (CABG).

2. Material and Method

After required approval and written informed consent, 50 patients posted for elective off pump CABG were included in the study.

Inclusion Criteria:

1. Patients posted for off pump CABG
2. EF more than 50%

Exclusion criteria:

1. Pre-existing renal disease
2. Pre-existing liver disease
3. Pre-existing respiratory disease
4. Patients with difficult intubation (Mallampatti grade- III, IV)⁴
5. Patients with neuromuscular disorders.
6. Patients who are already on beta-blockers.

50 patients were randomly and equally divided into two groups. Group RA (n=25) received Inj. Rocuronium 1 mg/kg as an Intubating agent followed after maintenance with Inj. Atracurium, while Group VV (n=25) received Inj. Vecuronium 0.2 mg/kg as an Intubating agent followed after maintenance with the same.

In all the patients, peripheral venous, radial and femoral arterial line and central venous access/PA catheter were secured under local anesthesia. All the patients were induced with Inj. Fentanyl 5µg/kg and Inj. Midazolam 0.1-0.15 mg/kg. Thereafter in group RA Inj. Rocuronium 1 mg/kg while in group VV Inj. Vecuronium 0.2 mg/kg was given. All the patients were maintained with O₂, Air and Isoflurane in a varying concentration (0.2-0.6%). In maintenance, group RA received Inj. Atracurium 0.5 mg/kg bolus after full recovery from Rocuronium as per the Train of Four (TOF) response when TOF showed 75% receptors are unoccupied followed by infusion of Atracurium at the rate of 0.5 mg/kg/hr along with Inj. fentanyl 2 µg/kg/hr and Midazolam 5µg/kg/hr. In group VV, Inj. Vecuronium incremental dose of 0.04 mg/kg as per TOF response along with Inj. Fentanyl 2 µg/kg and Inj. Midazolam 0.02 mg/kg every hour.

Neuromuscular block was monitored by acceleromyography with single twitch stimulation at supramaximal, square wave impulse of 0.2 ms duration, 1Hz, at the ulnar nerve using a TOF- monitor. After calibration to a baseline twitch height of 100%, the neuromuscular blocking drug was injected by an anesthesiologist. Timing of laryngoscopy was judged by the ease of ventilation, and jaw and upper airway tone. Jaw tone was assessed by attempting to open the patient's mouth, while upper airway tone was determined by the amount of jaw support necessary to maintain a patent airway. Laryngoscopy was performed with the patient in a standard position with McIntosh size 3 or 4 no. blade. Times from administration of neuromuscular blocking drugs to beginning of laryngoscopy and completion of tracheal intubation recorded. The anesthetist graded Intubating condition with excellent, good and poor condition. The view at laryngoscopy was also graded: 1- all of the larynx seen; 2-part of Vocal cords seen; 3-epiglottis only seen; 4- no structures identified.

Following parameters were observed at various sequences of events throughout the surgery. Such as Heart Rate

(HR), Mean Arterial Pressure (MAP), PA Pressure (PAP), SpO₂, Mixed venous saturation (SvO₂), Pulmonary Vascular resistance (PVR), Stroke volume (SV), Cardiac Output (CO). We have used PA catheter with continuous cardiac output monitor (CCO) with which we have observed above mentioned parameters. We have also used BIS monitor to measure depth of anesthesia in both the groups. Intra-operative fluid and Blood transfusion requirement, urine output were also compared in both the groups.

In post-operative period, time to awake after shifting, extubation time, any perioperative or postoperative complications, length of ICU stay and overall cost were compared in both the groups.

Data were analyzed by the Graphpad Prism V.6.0 computer statistic software using unpaired t-test, chi-square test. In all cases $P < 0.05$ was considered significant. Data presented were in terms of mean $\pm$ SD.

3. Observation & Results

A total of 50 patients were recruited for the study. There were no significant differences between the two groups in demographic data and duration of surgery (Table 1).

Table 1: Demographic Profile

Parameters	Group PF (n=25)	Group IF (n=25)	P Value	
Mean Age (years)	58.6 $\pm$ 11.9	56.06 $\pm$ 10.9	p>0.05	NS
Mean Height (cms)	158.53 $\pm$ 2.13	159.72 $\pm$ 1.62	p>0.05	NS
Mean Weight (kg)	68.53 $\pm$ 4.76	67.56 $\pm$ 3.76	p>0.05	NS
Sex (m/f)	14/11	13/12	-	-
Duration of surgery (min)	232.6 $\pm$ 27.2	238.6 $\pm$ 23.4	p>0.05	NS

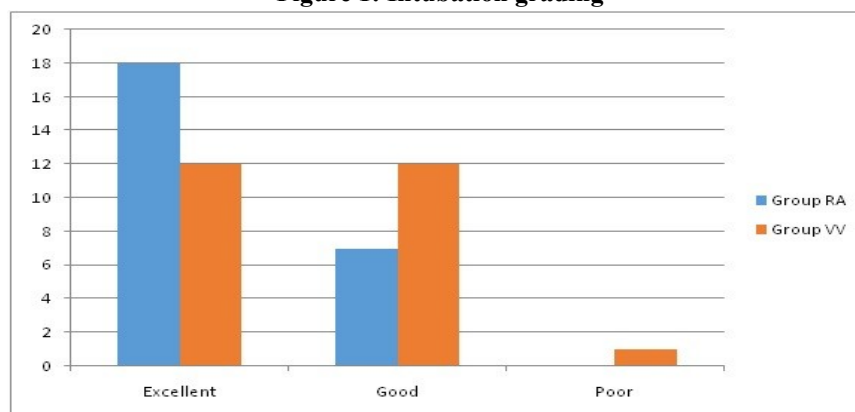
NS – Non Significant; S- Significant

Table 2: Intubating Condition parameters

Intubating condition parameters	Group RA (n=25)	Group VV (n=25)
Mallampati Grade I/II	16/9 (64/36%)	15/10 (60/40%)
Neuromuscular blocking drug to (sec)		
1. To start laryngoscopy	66 $\pm$ 6	164 $\pm$ 9
2. Completion of Intubation	76 $\pm$ 10	180 $\pm$ 12
View At Laryngoscopy (n)		
1. All of larynx seen	20 (80%)	19 (76%)
2. Part of larynx seen	5 (20%)	5 (20%)
3. Epiglottis only seen	0	1 (4%)
4. No structure seen	0	0

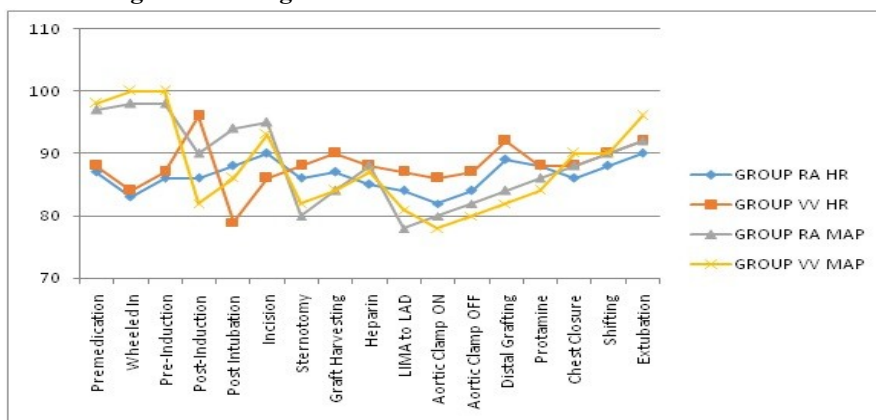
In group RA, laryngoscopy was not associated with laceration or injury to oral cavity while in group VV, we had one patient with blood clots in oral cavity which we have noticed while shifting the patient and most probably it was due to laceration effect enhanced by heparin.

Figure 1: Intubation grading



In one patient of group VV, it was difficult to visualize vocal cords, the only thing we could see was epiglottis though the patient was of Mallampatti Grade I, we had to use bougie for to facilitate intubation.

Figure 2: Change in Heart Rate and Mean Arterial Pressure



We observed stable heart rate and mean arterial pressure in group RA and observed fluctuation while intubation in group VV.

Figure 3: Change in Pulmonary Vascular resistance

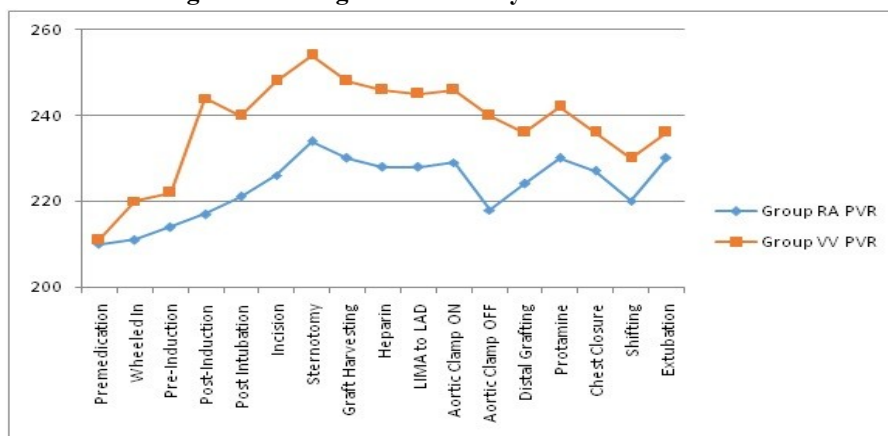


Figure 4: Change in Stroke Volume (SV)

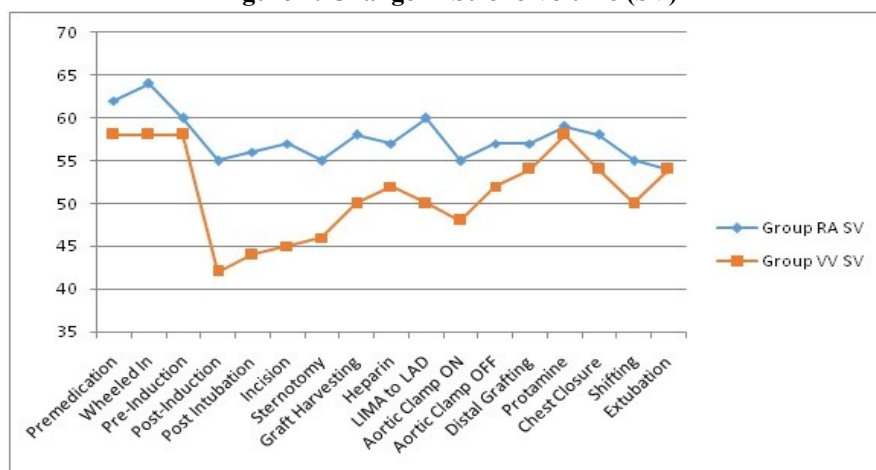
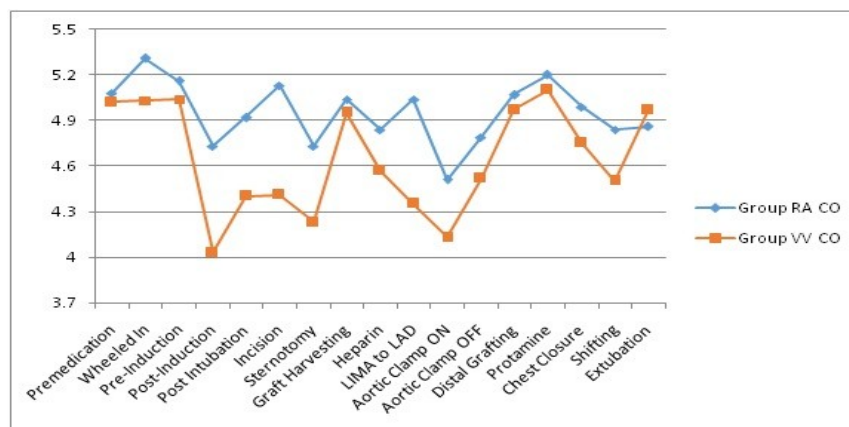
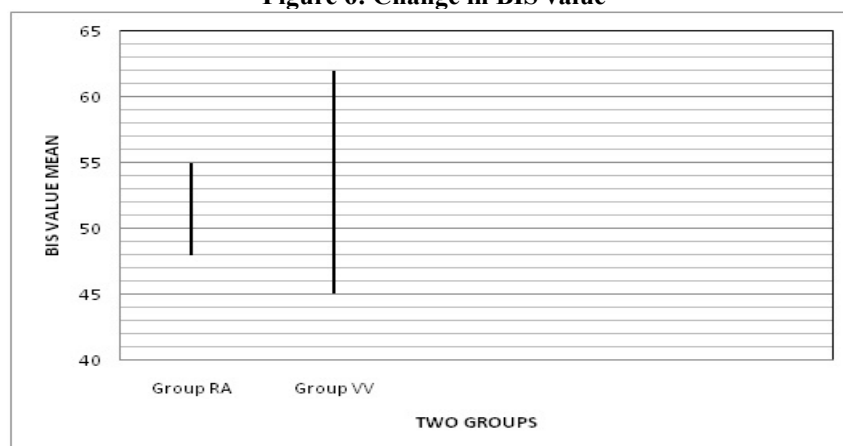


Figure 5: Change In Cardiac Output (CO)

Cardiac output = stroke volume x heart rate.

Figure 6: Change in BIS value

In VV group, isoflurane had to be given in varying concentration to maintain BIS value, while in group RA requirement of isoflurane was negligible and consistent.

Table 3: Perioperative & postoperative measures

Perioperative & postoperative measures	Group RA	Group VV
Intraoperative Fluid requirement	Avg. 1.7 Liter	Avg. 1.9 Liter
Blood Transfusion requirement	Avg. 13% patients	Avg. 16% patients
Time to Awake after shifting (min)	19.1 ± 2.4	73.5 ± 3.9
Extubation Time (min)	98.6 ± 7.9 (p<0.05)	237.9 ± 13.2
Length of ICU stay (hours)	62 ± 6.7 (p<0.05)	79 ± 7.2
SvO ₂	Lowest 65% Mean 72%	Lowest 62% Mean 70%
Incidence of post operative renal dysfunction (reduced urine output and elevated serum creatinine)	1 (4%)	1 (4%)
Incidence of LRTI	0	1 (4%)
Incidence of Atelectasis	0	1 (4%)

Extubation time in group RA with a patient of renal dysfunction was around 3.4 hours while in group VV it was 7.6 hours. In group VV, one patient had spurious respiratory secretions, we had to do frequent suctioning on ventilator and that patient developed LRTI (Lower respiratory tract infection) which was managed by antibiotics.

4. Discussion

Cardiac surgery has undergone revolutionary changes over the last two decades with invention of newer techniques, less invasiveness and better outcome. A faster recovery to normal function requires anaesthetic techniques which avoid a long-lasting impact on physiological functions. This can be influenced by how we manage airways, what sort of techniques we use for maintaining anaesthesia and analgesia. Rationale use of muscle relaxant also determines outcome of cardiac surgery.

Technique which offers extubation within 1-6 h postoperatively considered as "fast track" anesthesia described by Myles *et al*⁵. Most agree with the definition that "fast track" means extubation within 8 hours. Fast-track cardiac surgery is possible only if short-acting NMBDs (neuromuscular blocking drugs) are used and normal neuromuscular transmission is achieved at the end of surgery or at the time of extubation few hours after surgery.

NMB is necessary in cardiac surgery to facilitate smooth intubation conditions, mechanical ventilation and avoid patient movement, decrease oxygen consumption, and avoid shivering.⁶

Hemodynamic stability is very essential in cardiac surgery because coronary reserve is below normal in cardiac surgical patients. Any factor which augments myocardial O₂ demand by increasing heart rate, myocardial contractility or by changing blood pressure, SVR and PVR, is not considered good. It is therefore very necessary to avoid any agent including muscle relaxants which stimulates cardiovascular system and thus increase myocardial oxygen demand.⁷

Bartkowski *et al*⁸ compared time of onset of Rocuronium and Vecuronium and they have demonstrated that Rocuronium has early onset with better Intubating condition. In our study Time of onset after Rocuronium given and time to complete intubation was significantly lower as mentioned in previous studies as compared to Vecuronium. We found better Intubating condition with Rocuronium in comparison with Vecuronium.⁹ Rate of gastric inflation due to partial ventilation till the effect of the NMB achieved were significantly higher in Group VV because Vecuronium takes longer time to establish full neuromuscular blocking effect. We needed to insert Nasogastric tube in 20% of patient in group VV. In cardiac surgery, there are chances that injury occurred in nasopharynx while inserting NG tube may lead to profuse bleeding after heparin injection. Nasogastric tube is associated with nasal and maxillary sinus infection with radiological signs of inflammation.^{10,11}

In our study, there was slight increase in heart rate and mild decrease in MAP just after intubation with rocuronium while it was significant in case of Vecuronium. The reason behind that is mainly because of Rocuronium is three to six times less potent than Vecuronium as a NMB but is slightly more potent in blocking vagal response. Therefore slight increase in heart rate and slightly lower stroke volume just after induction led to maintained cardiac output and decrease in MAP. It is further justified by mild inotropic effect of Rocuronium as well.³

McCoy *et al*³ demonstrated that Vecuronium lacks chronotropic effect which may allow bradycardia to occur especially in patients receiving beta blocker or with high dose fentanyl anesthesia. To avoid this, we have premedicated all the patients with anticholinergic drugs. So because of that and also because of stress response we have observed significant increase in heart rate just after intubation in VV group as compared to RA group. In contrast, Rocuronium has mild sympathomimetic activity, with which it will have benefit over Vecuronium especially with high dose fentanyl anesthesia.

In our study we have observed significant fall in SV in group VV. As synchronized mechanical ventilation started after Vecuronium given, it takes time for to achieve full relaxation of diaphragm and intercostal muscles and lungs inflated by tidal volume, cannot displace diaphragm and intercostal muscles which are not fully relaxed and creates pressure effect on mediastinum leading to decrease in venous return and decrease in SV. While, in group RA, Rocuronium provides relaxation of diaphragm and intercostal muscles very soon which has positive impact in not producing pressure effect on mediastinum.³ Cardiac output remains in acceptable limits during induction in group RA than group VV. PVR was slightly increased in VV group after induction mainly because of difficulty in inflating the lungs with maintaining hemodynamics leading to increase in PCO₂ which has direct effect on PVR.¹²

BIS study showed that intermittent bolus doses of maintenance anesthesia drugs were associated with fluctuating

BIS value in group VV. Previous study demonstrates that delivery of anesthesia drug by infusion gives improved titration of the drug for BIS value.¹³

SvO₂ signifies balance between oxygen delivery and uptake by the tissue. If any of these two changes it gets reflected as change in SvO₂. In group VV, Vecuronium was given as intermittent bolus dose in maintenance. Though we

have repeated as per the Train of four response, plasma level of Vecuronium fluctuates resulting in subclinical shivering of the muscle leading to increased metabolic demand by tissues. In group VV, lowest value of SvO₂ was quite lower than RA group.¹¹

In group RA, better hemodynamics resulted in lesser fluid and blood transfusion requirement than group VV.¹²

In our study, we have used Atracurium infusion preceded by bolus dose in RA group. Flynn *et al* mentioned that Atracurium at slower infusion rate provide good surgical relaxation and adequate recovery from neuromuscular blockade after stopping. We experienced arousal of the patient immediately after shifting to post-operative ward which helped us in giving reversal agents timely. This results into shorten extubation time in group RA than group VV. Atracurium causes release of histamine if its infusion dosage exceeds 0.6 mg/kg/hr for prolonged period of time. We have used much lesser amount of Atracurium and that also for short duration.^{2,12}

Incidence of acute kidney injury (AKI) is around 4-5% and incidence of acute liver injury is around 0.5% after off pump CABG.^{14,15} Vecuronium is metabolized in liver and 70-85% eliminated by renal route. Principal metabolite of Vecuronium is 3-desacetylvecuronium which itself is potent neuromuscular blocker with prolong duration action even in comparison to Vecuronium, which depends on renal elimination fully. Rocuronium is metabolized in liver predominantly with no active metabolites. Elimination of Rocuronium is mainly through Liver (70-85%) and lesser extent by kidneys (15-30%). Atracurium is metabolized by Hofmann's elimination which is independent of hepatic or renal functions. In our study, by using Rocuronium followed by Atracurium we have tried to avoid accumulation of neuromuscular blocking drugs with single Intubating dose of Rocuronium. In group VV, induction and maintenance with Vecuronium had higher chances of residual neuromuscular blockade if would have been associated with renal or liver injury.

By using combination of Rocuronium and Atracurium we have tried to give clear benefit in above mentioned 5% of patient population with early extubation and shorten ICU stay in all the CABG patients.

5. Conclusion

Though Vecuronium is a gold standard in cardiac surgery as a neuromuscular blocking agent, Rocuronium as an Intubating agent followed by Atracurium infusion in off pump beating heart surgery resulted in better Intubating condition, stable hemodynamics and better post operative outcome than Vecuronium alone.

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References

1. Hemmerling TM, Prieto I, Choiniere JL, Basile F, Fortier JD. Ultra-fast-track anesthesia in off-pump coronary artery bypass grafting: A prospective audit comparing opioid-based anesthesia vs thoracic epidural-based anesthesia. *Can J Anaesth* 2004;51:163-8.
2. Ronald D. Miller, MD, Lars I. Eriksson, Lee A. Fleisher, MD, Jeanine P. Wiener-Kronish, MD and William L. Young. Miller's Anesthesia, 7th Edition.
3. Eamon McCoy, Venkat Maddineni, Peter Elliot, Rajinder Mirakhur, Ian Carson, Ronald Cooper. Hemodynamic effects of rocuronium during fentanyl anesthesia: comparison with Vecuronium. *Can J. Anesth.* 1993;40(8): 703-708.
4. Mallampatti SR, Gatt SP, Gugino LD, Desai SP. A clinical sign to predict difficult intubation. A prospective study. *Can. Anesthetist society Journal.* 1985;32:429-434.
5. Myles PS, Daly DJ, Djaiani G, Lee A, Cheng DC. A systematic review of the safety and effectiveness of fast-track cardiac anesthesia. *Anesthesiology* 2003;99:982-7.
6. Murphy GS, Szokol JW, Vender JS, Marymont JH, Avram MJ. The use of neuromuscular blocking drugs in adult cardiac surgery: Results of a national postal survey. *Anesth Analg* 2002;95:1534-9.
7. Kuhn C, Werdan K. Hemodynamic monitoring. In: Holzheimer RG, Mannick JA, editors. Surgical Treatment: Evidence-Based and Problem-Oriented. Munich: Zuckschwerdt; 2001.
8. Richard R. Bartkowski, Thomas A. Witkowski, Said Azad, Jennifer Lessin and Alexander Marr, Rocuronium Onset of Action: A Comparison with Atracurium and Vecuronium. *Anesth Analg* 1993;77(3):574-8.

9. Desmond P, Raman R, Idikula J Effect of nasogastric tubes on the nose and maxillary sinus. *Crit Care Med*.1991 Apr;19(4):509-11.
10. Svedjeholm R, Håkanson E, Szabó Z. Routine SvO₂ measurement after CABG surgery with a surgically introduced pulmonary artery catheter. *Eur J Cardiothorac Surg*. 1999;16(4):450-7.
11. Jon F. Berlaug, M.D., Jerome H. Abrams, M.D. Ian J. Gilmour, M.D. S. Rhiannon O'connor, M.D., David R. Knighton, M.D., And Frank B. Cerra, M.D. Preoperative Optimization of Cardiovascular Hemodynamics Improves Outcome in Peripheral Vascular Surgery A Prospective, Randomized Clinical Trial. *Ann. Surg*. 1991 (9):290-297.
12. Rosow C, Manberg PJ. Bispectral index monitoring. *Anesthesiol Clin North America*. 2001 Dec;19(4):947-66,
13. Flynn PJ, Hughes R, Walton B, Jothilingam S Use of atracurium infusions for general surgical procedures including cardiac surgery with induced hypothermia. *Br J Anaesth*.1983;55 Suppl 1:135S-138S.
14. Smith and R.S.G.Saand. Comparison of Intubating conditions after Rocuronium vs Vecuronium when timing of intubation is judged by clinical criteria. *Br. J. Anesth*.1998;80:235-237.
15. Joseph C Cleveland *et al*. Off-pump coronary artery bypass grafting decreases risk-adjusted mortality and morbidity. *The Annals of Thoracic Surgery* 72(4)2001:1282–1289.
16. Raman JS, Kochi K, Morimatsu H, Buxton B, Bellomo R. Severe ischemic early liver injury after cardiac surgery. *Ann Thorac Surg*. 2002 Nov;74(5):1601-6.