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Original Research Article

Comparison of rocuronium, vecuronium and atracurium in tiva for hemodynamic effects during beating heart bypass surgery

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Abstract

Aims: Patients requiring coronary artery bypass graft surgery are usually in compromised cardiac status and factors altering the myocardial oxygen demand and supply ratio, like, changes in heart rate, systolic diastolic and mean arterial blood pressure, myocardial contractility and vascular resistance may aggravate the underlying problem. Aim of our study was to compare the hemodynamic effects of neuromuscular blocking drugs like rocuronium, vecuronium and atracurium in patients undergoing elective coronary artery bypass graft (CABG) under Total intravenous anaesthesia.

Materials and Methods: Total of 90 cases were studied who were posted for elective beating heart CABG surgery, and were categorized into 3 groups with 30 patients in each group. Patients in group A were given vecuronium and group B and group C patients were administered with rocuronium and atracurium respectively, before intubation and for maintenance according to standard calculated doses. Hemodynamic parameters like HR, MAP, MPAP, PCWP, CI, SVI etc are measured at critical events and data analysed for assessing hemodynamic stability following use of the above said skeletal muscle relaxants.

Results: Overall vecuronium group was shown to be associated with decrease in HR, MAP, while other parameters were maintained. In rocuronium group there were increases in HR, MAP, MPAP, PCWP, CI, SVI, SVR, which were statistically significant but clinically not that significant.

In *atracurium* group there was decrease in HR, MAP, MPAP, PCWP, CI, SVI, SVR which were significant but clinically not that significant. From the present study it was concluded that vecuronium had a better and more cardiac favorable variables and more cardiovascular stability when compared to rocuronium and atracurium. Rocuronium was more cardio stable than atracurium. Vecuronium >Rocuronium >Atracurium (>=is better than).

Introduction

Coronary artery bypass graft surgery (CABG) commonly known as heart bypass surgery is a surgical intervention to reduce mortality and morbidity in patients suffering from significant coronary artery disease. Anaesthesia for coronary bypass surgery is challenging as we have to maintain the hemodynamic stability to avoid cardiovascular accident during surgery. Cardiovascular stability is an important determinant in choosing muscle relaxants. Although anaesthetic goals for bypass surgery are identical to any other procedures, drugs available for achieving these goals are affected by the unique requirements in these patients, like maintaining myocardial oxygen demand and supply ratio consequently strictly adhering to control Heart rate, pressure changes and left ventricular function. Commonly used Vecuronium is associated with bradycardia, while atracurium is associated with histamine release.[1-5] Another new long acting neuromuscular blocking agent rocuronium has faster onset of action and duration of action is similar to that of Vecuronium.[6,7] This drug belonging to aminosteroidal group has not been studied widely for it's cardiovascular stability, although some initial neuromuscular studies have raised few important concerns.[8,9]

Neuromuscular blocking drugs interact with nicotinic and muscarinic cholinergic receptors within the sympathetic and parasympathetic nervous system and at the nicotinic receptors of the NM junction. Dose response ratios can be derived by comparing the potencies of muscle relaxants in blocking the neuromuscular junction at muscle (ED 95) with their potencies in blocking parasympathetic or sympathetic ganglion transmission (ED). The higher the dose ratio, the lower the likelihood or the greater the safety ratio for the occurrence of the particular autonomic effect. The side effect is absent (none) in clinical practice if the safety ratio is 3 or 4, moderate if 2 or 3, and strong or prominent if ratio is 1 or less. The side effect of histamine release is most

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often noted after administration of benzylisoquinolinium (Atracurium) class of muscle relaxants.

Aim of our study was to compare the hemodynamic effects of neuromuscular blockers like atracurium, vecuronium and rocuronium in patients undergoing bypass surgery under total intravenous anaesthesia (TIVA).

Materials and Methods

We conducted this prospective randomized controlled study after clearance from institutional ethical committee. Patients posted for elective CABG surgery, belonging to ASA physical status classification II and III, aged between 30 to 60 years, of both the sex, weighing between 45 to 70 kgs were included in the study. All the patients were on beta blocker therapy. Patients who were <45 kgs or > 70 kgs, patients with LVEF < 35%, patients with renal or hepatic derangements and patients having COPD and asthma were excluded from the study. Total of 90 cases were studied who were posted for elective beating heart CABG surgery, and were categorized into three groups of 30 each. Sample size was estimated using a reference study, with type I error at 5% level of significance and 80% power of study.

30 patients were included in each group to round off, after we derived 28 patients in each group through sample size estimation. Patients under the study underwent thorough preoperative assessment and clinical examination including necessary investigations. Patients were counselled about the proposed surgery, anaesthesia procedure and drugs being used in locally spoken language and a well informed consent was obtained. All the patients were given anti anxiety prophylaxis with tab lorazapam 2mg and aspiration prophylaxis with tab ranitidine 150 mg. Premedication was given in the ICU room under cardiac observation and included intramuscular inj midazolam (0.04mg/kg), inj pentazocin (0.3mg/kg), inj glycopyrrolate (5 mcg/kg) and inj phenargan (0.5mg/kg).On the day of surgery basic monitors were attached and crystalloids were started.

In group A patients were induced with 5mcg per kg of injection fentanyl and 0.04mg per kg of injection midazolam. Under direct laryngoscopic vision tracheal intubation was done after giving inj vecuronium (0.08mg/kg) as skeletal muscle relaxant. Anaesthesia was maintained on O2+N2O (50:50) with continuous infusion of inj fentanyl (1mcg /kg/min)+inj midazolam (0.02mg/kg/min)+inj vecuronium (0.005-0.0012 mg/kg/min).

Group B patients were induced with 5mcg per kg of injection fentanyl and 0.04 mg per kg of injection midazolam. Under direct laryngoscopic vision tracheal intubation was done after inj rocuronium (0.6mg/kg) as skeletal muscle relaxant. Anaesthesia was maintained on O2+N2o (50:50) and continuous infusion of inj fentanyl (1 mcg/kg/min)+inj midazolam (0.02mg/kg/min)+inj rocuronium (0.003-0.008mg/kg/min).

Group C patients were induced with 5mcg per kg of injection fentanyl and 0.04mg per kg of midazolam. Under direct laryngoscopic vision tracheal intubation was done after inj atracurium (0.05mg/kg) as skeletal muscle relaxant. Anaesthesia was maintained on O2+N2O(50:50) with continuous infusion of inj fentanyl (1mcg /kg /min) +inj midazolam (0.02mg/kg/min)+inj atracurium (0.006-0.012 mg/kg/min).

Arterial line and central venous line were secured and connected to monitor. cardiovascular observations were done and cardiovascular parameters like heart rate, Mean arterial pressure, mean pulmonary artery pressure, pulmonary capillary wedge pressure, central venous pressure, cardiac index, stroke volume index, systemic vascular resistance and pulmonary vascular resistance were monitored at every 10 minutes and at vital times of preinduction, after the induction, after tracheal intubation, during skin incision, during sternotomy, sternotomy closure and skin closure.

Observations at each event and every 10 min were done with PNS and results were noted and according to results, adjustment of muscle relaxant was done. Obtained data was analysed using appropriate statistical tests and computerized tables.

Table 1: Comparison of heart rate in study groups

Heart Rate	Group A	Group B	Group C	F value	P value
	Mean ± SD (n=30)	Mean ± SD (n=30)	Mean ± SD (n=30)		
Pre induction		66.47±1.65	67.30±2.94	24.72	<0.0001
Post Induction	64.87±2.81	68.8±1.81	66.13±3.61	172.69	<0.0001
Intubation	63.87±2.81	66.7±1.93	64.13±3.58	398.23	<0.0001
Skin incision	60.87±2.81	65.73±1.86	64.23±3.54	682.86	<0.0001
Sternotomy	58.06±2.58	67.73±1.86	62.23±3.54	1010.9	<0.0001
SOS if significant change	58.07±2.58	72.07±2.21	60.27±3.46	759.07	<0.0001
Sternum closure	57.06±2.58	73.97±1.94	59.27±3.42	669.75	<0.0001
Skin closure	59.10±2.63	74.07±1.84	59.27±3.42	384.47	<0.0001

Table 2: Comparision of MAP in study groups

MAP	Group A	Group B	Group C	F value	P Value
	Mean ± SD(n=30)	Mean ± SD(n=30)	Mean ± SD(n=30)		
Pre induction	97.73±0.78	96.50±1.19	98.77±1.65	5.41	<0.01
Post induction	99.73±0.78	97.50±1.19	96.03±1.71	199.4	<0.0001
Intubation	96.70±0.75	98.53±1.14	95.77±1.69	51.02	<0.0001
Skin incision	94.17±0.75	99.53±1.14	93.83±1.58	122.98	<0.0001
Sternotomy	94.70±0.75	101.53±1.14	91.83±1.58	693.84	<0.0001
SOS if significant change	95.70±0.75	103.53±1.14	89.83±1.58	528.5	<0.0001
Sternum closure	93.67±0.80	104.53±1.14	88.88±1.58	787.73	<0.0001
Skin closure	94.60±0.80	104.53±1.14	86.83±1.58	1396.89	<0.0001

Table 3: Comparision of MPAP in study groups

MPAP	Group A	Group B	Group C	F value	P value
	Mean ± SD(n=30)	Mean ± SD(n=30)	Mean ± SD(n=30)		
Pre induction	21.21±0.76	21.10±1.21	22.27±0.+94	134.06	<0.0001
Post induction	20.21±0.76	23.07±0.87	21.32±0.92	745.76	<0.0001
Intubation	20.20±0.76	24.22±0.76	20.32±0.91	1577.87	<0.0001
Skin incision	19.20±0.76	26.25±0.76	19.32±0.91	984.29	<0.0001
Sternotomy	19.20±0.76	27.22±0.76	18.32±0.92	41115.75	<0.0001
SOS if significant change	18.17±0.79	29.21±0.76	16.30±0.92	4124.64	<0.0001
Sternum closure	18.17±0.79	30.21±0.76	15.30±0.92	3326.08	<0.0001
Skin closure	18.17±0.79	32.21±0.76	14.30±0.92	2214.85	<0.0001

Table 4: Comparision of PCWP in study groups

PCWP	Group A	Group B	Group C	F value	P value
	Mean ± SD(n=30)	Mean ± SD(n=30)	Mean ± SD(n=30)		
Pre induction	11.80±1.21	12.03±0.93	12.63±1.09	309.28	<0.0001
Post induction	12.23±1.04	16.30±0.93	13.63±1.02	228.34	<0.0001
Intubation	11.67±1.06	16.30±0.73	12.77±1.02	185.64	<0.0001
Skin incision	11.43±0.97	15.30±0.77	10.77±1.02	208.39	<0.0001
Sternotomy	11.40±0.97	14.30±0.73	8.77±1.02	274.39	<0.0001
SOS if significant change	10.97±1.10	14.30±0.73	8.77±1.02	251.23	<0.0001
Sternum closure	10.27±0.87	15.30±0.73	9.77±1.02	362.01	<0.0001
Skin closure	10.13±0.86	15.30±0.73	9.77±1.02	372.23	<0.0001

Table 5: Comparision of SVR in study groups

SVR	Group A	Group B	Group C	F value	P Value
	Mean ± SD(n=30)	Mean ± SD(n=30)	Mean ± SD(n=30)		
Pre induction	1666.77±82.12	1670.33±35.25	1671.07±25.60	0.06	>0.05
Post induction	1650.87±81.16	1645.37±35.27	1601.07±25.61	7.90	<0.0001
Intubation	1618.87±82.57	1588.70±38.46	1550.73±25.91	11.69	<0.0001
Skin incision	1518.87±82.57	1488.73±38.47	1450.9±26	11.63	<0.0001
Sternotomy	1471.53±79.83	1442.50±42.29	1350.9±26.00	40.37	<0.0001
SOS if significant change	1471.53±79.83	1442.50±42.29	1300.9±26.00	84.87	<0.0001
Sternum closure	1491.23±78.92	1462.83±42.21	1300.9±26.00	109.25	<0.0001
Skin closure	1480.23±102.77	1492.50±41.79	1350.9±26	42.66	<0.0001

Results

Mean age of patients in group A, group B axw2qqnd group C was 51.33, 52.60 and 52.07 years respectively and by Z test difference was statistically insignificant significant. Similarly all patients were comparable with respect to sex distribution (Chi square test), weight and height. In group A patients heart rate reduced by 10% (P<0.001) compared to pre operative values, which was statistically significant but clinically insignificant. In group B there was a rise in heart rate by 15% (P <0.001) when compared to preoperative

values, again which is statistically significant but clinically insignificant. In group C heart rate reduced by 12% (P <0.001) when compared to preoperative heart rate, which was statistically significant but clinically insignificant but clinically insignificant. Results from the observations of Mean arterial pressure (MAP) showed some clinically insignificant but statistically significant changes. Among group A patients MAP reduced by 4% when compared to basal values (P>0.05), which was statistically not significant. But in group B patients there was a rise in MAP by 13% (P <0.001), which was clinically insignificant but statistically significant finally In group C there was a decrease in MAP by 10% (P <0.001) which was clinically insignificant but statistically significant.

Like MAP, change in mean pulmonary artery pressure (MPAP) was also statistically significant. Among Patients in group A there was a reduction in MPAP by 5%, which was statistically not significant. In group B there was a rise of MPAP by 17%, which was clinically insignifican but statistically significant. Finally Group C patients showed a fall in MPAP by 14%, which was clinically insignificant but statistically significant. Likewise there were clinically insignificant but statistically significant changes in pulmonary capillary wedge pressure (PCWP).

In group A fall in PCWP was only 4% and was statistically insignificant, where as among group B there was a statistically significant rise in PCWP by 11%. Group C patients showed a fall PCWP by 15% which was statistically significant. Measurement of Central venous pressure did not show any statistically significant changes. Cardiac index measurements showed clinically insignificant but statistically significant changes, while group A patients had 3% reduction in cardiac index which was statistically not significant, group B patients showed statistically significant but clinically insignificant rise in cardiac index by 11%. Finally group C patients had a fall in cardiac index by 10%, which was only statistically significant. Similarly there were statistically significant changes in Stroke volume index, in group A there was a reduction of stroke volume index by only 4%, while group B patients had a rise of stroke volume index by 19%, which was statistically as well as clinically significant. In group C there was a fall in stroke volume index by 17%, which was statistically significant. Systemic vascular resistance also was variable in three groups, while group A patients showed statistically insignificant reduction, group B patients showed statistically significant but clinically insignificant rise. In group C there was a statistically significant but clinically insignificant reduction in SVR. Both group A and group B patients did not experience any statistically significant change in pulmonary vascular resistance, while there was a statistically significant but clinically insignificant reduction in pulmonary vascular resistance by 10% in group C patients.

Discussion

Patients with compromised cardiac reserve are very vulnerable to any factor which alter myocardial oxygen demand and supply ratio. Factors causing elevation in heart rate, blood pressure and cardiac contractility along with factors altering systemic and pulmonary vascular resistance will alter this balance and can lead to increased chances of intraoperative and postoperative myocardial ischemia and subsequently increased incidence of postoperative morbidity and mortality.[10,11] Present study showed that neuromuscular blocking agents like rocuronium, vecuronium and atracurium were associated with important hemodynamic changes that were statistically significant.

The increase in heart rate among rocuronium group can be related to its vagal blockade tendency and reduction in heart rate among atracurium group patients can be related to its tendency to liberate histamine. Reduced heart rate among group A patients cannot be attributed to histamine release or vagal stimulation. Our findings are consistent and comparable to study conducted by Robertson EN, Hull JM, Verbeek AM, Booij LH,[12] where they observed an increase in HR by 30-35% in rocuronium group. Heart rate reduction in atracurium group was significant but was not significant in vecuronium group. Similar results were noted by M. G. Booth, B. Mars, F. M. M. Bryden, E. N. Robertson, W. L. M. Baird.[13]

Mean arterial pressure increased in group B, while it was low in group C. Eamon P, McCoy and colleagues studied hemodynamic effects of rocuronium during fentanyl anaesthesia and compared with vecuronium, where they noticed 17% increase in MAP with rocuronium and statistically insignificant fall with vecuronium. Mean pulmonary artery pressure (MPAP) was significantly high with rocuronium and significantly low with atracurium in our study. R. S. Emmott, B. J. Bracey.[15] conducted a study on cardiovascular effects of muscle relaxants and observed that rocuronium was associated with rise and atracurium was associated with fall in mean pulmonary artery pressure.

Pulmonary capillary wedge pressure (PCWP) was high in rocuronium group and low in atracurium group, and these findings were comparable with the observations by Gallo JA, Cork RC, Puchi.[16] They observed that atracurium was associated with significant reduction in PCWP due to histamine release and concluded that vecuronium may be advantageous over atracurium when cardiovascular stability is crucial.

Cardiac index (CI) measurements revealed significant fall with atracurium and significant rise with rocuronium, which again were similar to the results noticed by Peter Elliott, Ian W. Carson and Ronald A. Cooper.[17] They observed 11% increase in CI with rocuronium and 15% reduction in CI with atracurium. Similar study also revealed that stroke volume index (SVI) was low with atracurium group and high among rocuronium group and we also noticed the similar results. While observing systemic vascular resistance (SVR) we found that there was a significant rise in rocuronium group and fall in atracurium group, Robertson EN, Hull JM, Verbeek AM, Booij LH[18] also noticed similar results. Group C showed statistically significant reduction in pulmonary vascular resistance while it was maintained in other groups. Overall vecuronium

group was shown to be associated with decrease in HR, MAP, while other parameters were maintained. These changes are more favorable to a patient with ischemic heart disease, leading to a situation of more cardiovascular stable property of drug vecuronium. In rocuronium group there were increases in HR, MAP, MPAP, PCWP, CI, SVI, SVR, which were statistically significant but clinically not that significant where there was a need to counter act these effects by other pharmacological interventions. In atracurium group there was decrease in HR, MAP, MPAP, PCWP, CI, SVI, SVR which were significant but clinically not that significant where there was a need to counter act these effects by other pharmacological interventions. Compared to vecuronium, the changes seen with use of atracurium were far more in magnitude leading to the adverse effects on the ischemic heart. By decreasing heart rate and MAP to greater extent, the failing heart needs to increase it's contractility in order to compensate for the fall in HR and MAP and by doing so, the oxygen demand of heart may further increase and lead to more ischemic damage.

Conclusion

From the present study it was concluded that vecuronium had a better and more cardiac favorable variables and more cardiovascular stability when compared to rocuronium and atracurium. Rocuronium was more cardio stable than atracurium. Vecuronium >Rocuronium >Atracurium (>=is better than).

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