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Research Article

Comparison of effects of rocuronium bromide versus vecuronium bromide on hemodynamic parameters during anaesthesia for elective surgical procedures

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ABSTRACT

Background: Understanding haemodynamic effects of muscle relaxants may help us in selection of most appropriate muscle relaxant in a given case after considering preoperative cardiac status, preoperative medications, anaesthetic drugs to be used, nature of surgery and desirable intraoperative hemodynamics. Hemodynamic effects of rocuronium are not as clear as vecuronium. Present study was conducted to compare haemodynamic parameters during general anaesthesia for elective surgical procedures with vecuronium vs. rocuronium as muscle relaxant.

Methods: Haemodynamic effects of vecuronium 0.15 mg/kg and 0.9 mg/kg of rocuronium was evaluated in patients (25 patients in each group) undergoing elective surgical procedures not lasting more than two hours. During this study period patients were evaluated for heart rate (HR), systolic BP (SBP), diastolic BP (DBP) and mean arterial pressure (MAP).

Results: When both groups were compared, degree of fall in heart rate was more in vecuronium group (V group) compared to rocuronium group at all-time intervals after administration of drug. The fall in mean heart rate in V group was significant at two minutes after administration of muscle relaxant when compared to R group i.e.77.12±9.96 vs. 85.04±12.82 ($p<0.05$) and was highly significant at 3 minutes after administration of drug i.e. 76.12±9.67 vs. 85.44±12.47 ($p<0.001$). After induction and administration of vecuronium or rocuronium there was fall in systolic blood pressure, diastolic blood pressure and mean arterial pressure in both the groups when these parameters were recorded before laryngoscopy with slightly more but comparatively non-significant fall in these parameters in vecuronium group. Intraoperatively these parameters were comparable in both groups and no significant difference from baseline was observed in these parameters in both groups thereby showing good haemodynamic stability.

Conclusions: Vecuronium is associated with greater decrease in heart rate than rocuronium in clinical doses. No increase in heart rate was observed with rocuronium in doses used. In all other aspects (SBP, DBP, MAP) haemodynamic effects were similar in both groups with slightly greater but non-significant fall observed after administration of vecuronium group.

Keywords: Vecuronium, Rocuronium, Heart rate, Haemodynamic effects

INTRODUCTION

Hemodynamic stability is an important aspect of anaesthesia care. Anaesthesia has tendency to produce significant hemodynamic changes especially during induction and intubation. Also many of the factors like reflex vagal activity during surgeries like strabismus surgery, laparotomy[1,2] and concurrent use of various anaesthetic agents can significantly alter hemodynamics during the course of anaesthesia. So, hemodynamic effects of the drug remain important criteria while selecting neuromuscular blocking agent during

anaesthesia especially in selected cases where maintaining hemodynamic parameters within specified range is critical.

The older neuromuscular blocking agents (e.g. tubocurarine, alcuronium, and pancuronium) are well known for their hemodynamic effects produced either by affecting autonomous nervous system or by Histamine release. Pancuronium is of particular importance which significantly increases heart rate and mean arterial pressure due to its sympathomimetic and vagolytic property. Introduction of vecuronium and atracurium considerably improved flexibility in clinical administration of muscle relaxants due to their intermediate duration of action, favourable recovery and hemodynamic stability. However reports of bradycardia have appeared in literature in patients receiving vecuronium along with high dose of opiates,[3] β blocker therapy and in procedures with reflex vagal activity(strabismus surgery, laparotomy).[4] This may be due to inability of vecuronium to counterbalance various negative chronotropic effects.

Rocuronium bromide, in view of its hemodynamic effects is not as clear as vecuronium. It causes increase in heart rate though not as marked as pancuronium and is clinically acceptable.[5] This positive chronotropic effect may be beneficial under situation where negative chronotropic effects are likely to be predominant as in strabismus surgery and high dose opioid anaesthesia.[6,7] However few studies showed significant increase in heart rate after rocuronium administration.[8]

Present study was conducted to compare haemodynamic parameters (HR, SBP, DBP, MAP) during general anaesthesia for elective surgical procedures with vecuronium vs. rocuronium as muscle relaxant.

METHODS

The present study was conducted in tertiary care institute, after ethics committee approval. This was prospective randomized controlled trial done on patients undergoing elective surgeries requiring general anaesthesia not lasting for more than two hours and with minimal blood loss. Two groups were done i.e. group 'V' receiving vecuronium (Neovec, Neon India) and group 'R' receiving rocuronium (Esmeron, Organon India Pvt Ltd). Each group had 25 patients. ASA grade I and II patients of either sex in age group of 18 to 65 having MPC (Mallampatti class) grade I and II undergoing elective surgery of less than 2 hours duration with blood loss less than five hundred ml were included in study.

Patients having history of neuromuscular disorder, cardiovascular disorder, hypertension, diabetes mellitus, obesity, difficult airway or previous history of difficult intubation, patients who were on medications which are likely to affect hemodynamic variables e.g. β blockers, calcium channel blockers and patients undergoing intra-cavitory surgical procedures with prominent sympathetic or parasympathetic responses like cholecystctomy, laparotomy, strabismus surgery were excluded from study.

All patients received tab diazepam 10 mg and tab ranitidine 150 mg, a night prior to surgery.

After detailed pre-anaesthetic check-up and valid informed written consent, patients were shifted to operating room. Monitors including ECG, pulse oximeter and non-invasive blood pressure cuff were attached and baseline parameters including heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure were recorded. An intra-venous access was obtained and ringer lactate started. Patients were pre-medicated with IV inj midazolam 0.03 mg/kg and inj fentanyl 2 mcg/kg. After five minutes of premedication and oxygenation, patients were induced with 5 mg/kg of thiopentone sodium. After two minutes of induction patients were paralysed in 'R' group with 0.9 mg/kg of rocuronium IV and Inj vecuronium 0.15 mg/kg IV in 'V' group. Patients were ventilated for three minutes using oxygen and nitrous oxide (50:50) after which patients were intubated by trained anaesthesiologist with proper sized cuffed PVC endotracheal tube. Confirmation of endotracheal tube was done clinically and using $ETCO_2$. Maintenance was done with oxygen-nitrous (40:60) and isoflurane 1% with intermittent positive pressure ventilation using circle system. Maintenance doses of muscle relaxant were given in respective group using rocuronium 0.1 mg/kg IV in 'R' group and vecuronium 0.02 mg/kg in 'V' group every 45 minutes. Inj diclofenac sodium 1.5 mg/kg was given for postoperative analgesia just after induction of anaesthesia. Reversal was done using neostigmine 0.05 mg/kg and glycopyrrolate 0.008 mg/kg and patient were extubated. Patients were observed in recovery room for one hour. During this study period patients were monitored for heart rate (HR), systolic BP (SBP), diastolic BP (DBP) mean arterial pressure (MAP), oxygen saturation and temperature. Intubating conditions during laryngoscopy were also noted. The parameters were recorded preoperatively before pre-medication (Baseline), 5 minutes after premedication, 2 minutes after induction with thiopentone immediately before giving muscle relaxant, 1 minute, 2 minute, 3 minutes after administration of muscle relaxant, immediately 1,3,5 minutes after laryngoscopy and intubation and every five minutes intraoperatively up to 2 hrs if surgery is prolonged. Intubating conditions were assessed by Goldberg et al scale.[9] Intraoperative hypotension (MAP<30% of preoperative value) was treated using intravenous fluids and Inj mephentermine while bradycardia HR<50 was treated with suitable doses of atropine. Hypertension was treated with increasing depth of anaesthesia with increasing isoflurane concentration and fentanyl 0.5 mcg/kg while tachycardia (HR>100) was treated with fluid challenge and fentanyl 0.5 mcg/kg.

RESULTS

This study included 50 patients which were divided into two groups of 25 each i.e. R group and V group. All demographic parameters were comparable. Intubating conditions were also excellent and similar in both groups. All baseline parameters including heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure were comparable. After administration of drug, change in mean heart rate was not significant when compared to baseline in both groups. However when both groups were compared, degree of fall in heart rate was more in V group compared to R group at all-time intervals after administration of drug. The fall in mean heart rate in V group was significant at two minutes after administration of muscle relaxant when compared to R group i.e. 77.12±9.96 vs 85.04±12.82($p<0.05$) and was highly significant at 3 minutes after administration of drug i.e. 76.12± 9.67 vs. 85.44± 12.47 ($p<0.001$) (Table 1).

The baseline mean heart rate in 'R' group was 85.52±12.29. After administration of drug at 1 minute, 2 minute, 3 minute there was slight decrease in heart rate which was not significant($p>0.05$). In 'V' group baseline heart rate was80.56±8.95. The mean heart rate decreased at all times with maximum decrease at 3 minutes by 5.51%, however decrease in heart rate was not significant when compared to baseline($p>0.05$).

Table 1: Comparison of mean heart rate between 'R' group and 'V' group after administration of drug.

Heart rate/minute (Mean±SD)			
Interval	**'R' group (n=25)**	**'V' group (n=25)**	**Significance**
Baseline	85.52±12.29	80.56±8.95	NS
1 minute	85.44±12.78	78.08±9.6	NS
2 minutes	85.04±12.82	77.12±9.96	($p<0.05$) S
3 minutes	85.44±12.47	76.12±9.67	($p<0.001$) HS

Unpaired't' test, NS- not significant, S- significant, HS-highly significant.

During laryngoscopy rise in mean heart rate was statistically comparable in both groups.

Intraoperatively vecuronium showed more tendencies to fall in heart rate compared to rocuronium.

Table 2: Change in mean heart rate from baseline in 'R' and 'V' group after administration of drug.

	'R' group (n=25)			'V' group (n=25)		
Interval	**Heart rate/minute (Mean±SD)**	**% Change**	**Significance**	**Heart rate/minute (Mean±SD)**	**%Change**	**Significance**
Baseline	85.52±12.29	-	-	80.56±8.95	-	-
1 minute	85.44±12.78	-0.09	NS	78.08±9.6	-1.84	NS
2 minute	85.04±12.82	-0.56	NS	77.12±9.96	-4.27	NS
3 minute	85.44±12.47	-0.09	NS	76.12±9.67	-5.51	NS

Unpaired't' test, NS-not significant, '+'-% increase from baseline, '_'% decrease from baseline.

Table 3: Comparison of mean heart rate between R and V group during intra operative period.

Heart rate/minute (MEAN±SD)			
Interval	**'R' group, (n=25)**	**'V' group, (n=25)**	**Significance**
Baseline	85.52±12.29	80.56±8.95	NS
Incision	86.64±11.47	79.92±9.63	($P<0.05$) S
5 minutes	87.16±11.09	78.16±8.29	($P<0.05$) S
10 minutes	85.28±11.92	76.52±8.85	($p<0.001$) HS
30 minutes	81.08±11.56	71.12±9.95	($p<0.001$) HS
60 minutes	77.60±14.21	72.16±11.11	NS
90 minutes	78.04±16.34	74.38±11.33	NS
120 minutes	75.82±13.31	73.56±8.85	NS
Mean intra operative heart rate	82.03±13.31	75.97±10.15	NS

Unpaired't' test, NS-Not significant, S- significant, HS- highly significant.

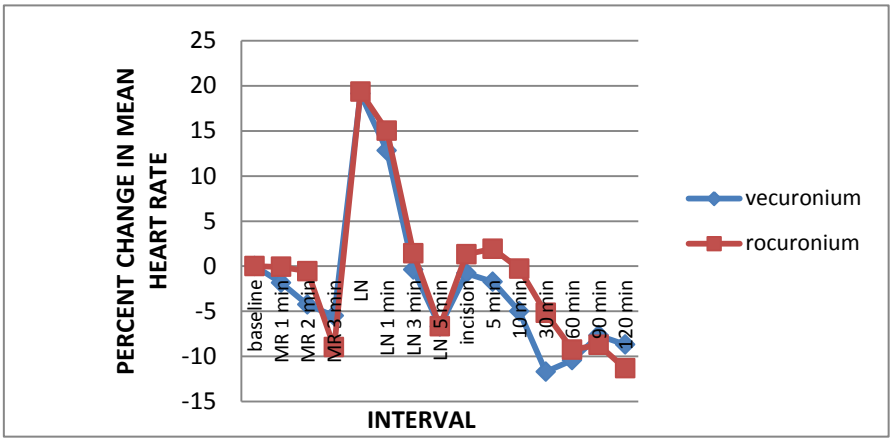

Figure 1: Comparison of percent change in mean heart rate between 'R' group and 'V' group.

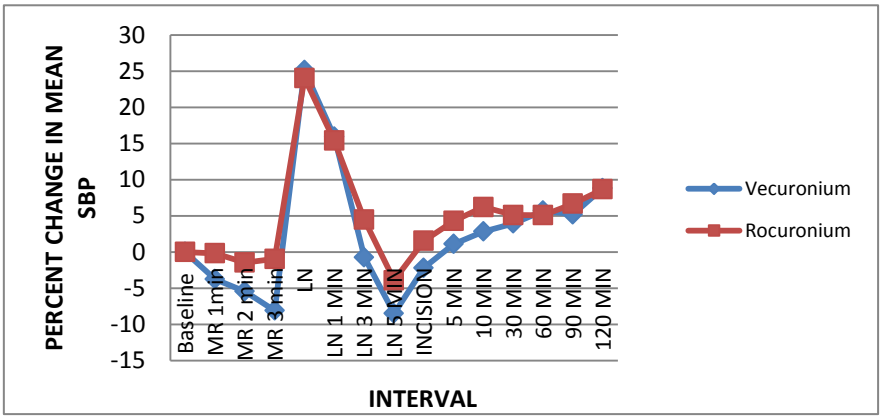

Figure 2: Comparison of percent change in mean SBP between 'R' group and 'V' group.

Table 4: Comparison of change in mean diastolic BP between R group and V group after laryngoscopy.

Interval	R group, (N=25)	V group, (N=25)	Significance
Baseline	71.84±7.06	71.36±11.42	NS
During laryngoscopy	90.4±9.03	89.68±11.77	NS
1 minute	90.28±8.98	83.6±7.49	(p<0.001) HS
3 minutes	74.24±10.7	70.08±7.31	NS
5 minutes	66.4±11.06	66.08±8.9	NS

Fall in systolic blood pressure was comparable in both groups after administration of drug. Both groups were comparable regarding change in systolic blood pressure during and after laryngoscopy. Both groups were comparable regarding change in systolic blood pressure at all times intraoperatively.

Fall in diastolic BP was comparable in both groups after administration of drugs. During laryngoscopy both groups had shown rise in diastolic BP which was comparable while at one minute after laryngoscopy rise in diastolic BP in R group as compared to V group was highly significant i.e. 90.28±8.98 vs. 83.6±7.49 (p<0.001).

Both groups were comparable regarding change in mean diastolic blood pressure at all times intraoperatively.

Both groups were comparable regarding change in mean arterial pressure at all times intraoperatively.

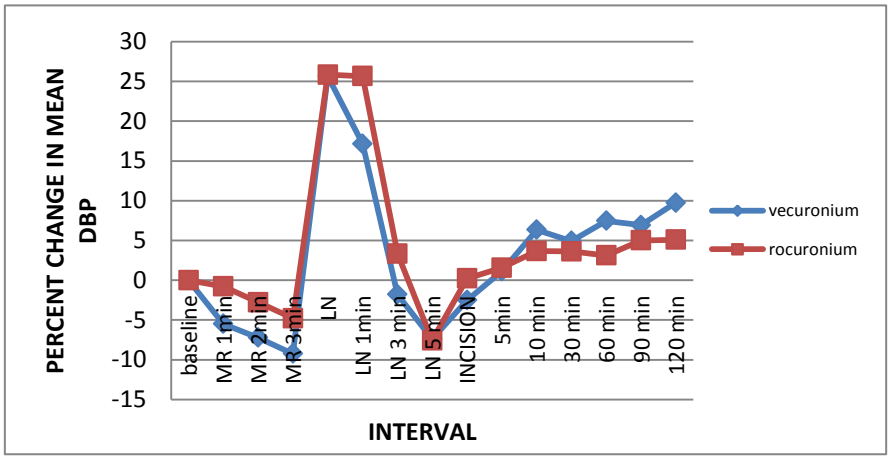

Figure 3: Comparison of percent change in mean DBP between 'R' group and 'V' group.

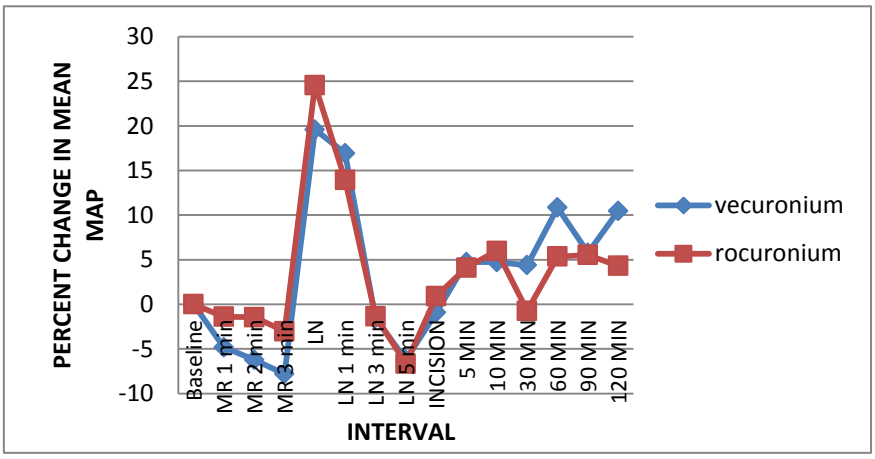

Figure 4: Comparison of percent change in mean map between 'R' group and 'V' group.

Thus we found that vecuronium is associated with greater decrease in heart rate than rocuronium in clinical doses. No increase in heart rate was observed with rocuronium in doses used. Other hemodynamic effects were similar in both groups with slightly greater but no significant fall in heart rate observed after administration of vecuronium.

DISCUSSION

Neuromuscular blocking drugs can have effects on hemodynamic parameters which can be either due to autonomic effects or histamine release property of the drugs. In our study we compared rocuronium and vecuronium regarding their cardiovascular effects. vecuronium is devoid of any autonomic effects or histamine release property. However, several case reports in literature have described bradycardia after administration of vecuronium. The studies have found that vecuronium itself does not cause decrease in heart rate (Cozantis et al).[10] The decrease in heart rate is seen when it is administered concurrently with other anaesthetic agents such as opioids, halothane (Salmenpern et al),[3] in surgical procedures with reflex vagal activity (laparotomy, cholecystctomy) (C.P.J. Morton et al).[4] The proposed mechanism can be failure of vecuronium to counterbalance the negative chronotropic effects. Rocuronium as against VECURONIUM is associated with mild increase in heart rate at doses 3-4 times ED95 (J.B.Stevens et al)[11] which is clinically acceptable. However some studies have found significant increase in heart rate (Booth et al).[8] The proposed mechanism can be its vagolytic action because of its lower vagal to neuromuscular blockade ratio (Muir et al).[12]

In present study, we compared haemodynamic parameters with three times ED95 doses of IV rocuronium bromide i.e. 0.9 mg/kg vs IV vecuronium bromide 0.15 mg/kg used as muscle relaxant for intubation and subsequently maintenance doses intraoperatively. Similar doses were used by many authors in their study (G.D. Shorten et al,[13] E.N. Robertson et al,[5] J.B. Stevens et al[11]).

We avoided using anticholinergics as these drugs because of their vagolytic effect may increase heart rate. Patients were premedicated with inj midazolam and inj fentanyl. After five minutes of premedication and oxygenation, patients were induced with inj thiopentone sodium. After two minutes of induction patients were administered

either vecuronium or rocuronium in respective groups. After administrations of study drug all haemodynamic parameters were recorded at 1 min interval for 3 minutes while patients were being ventilated with oxygen and nitrous oxide (50:50). Thereafter parameters were recorded 1, 3, 5 minutes after laryngoscopy and intubation and every five minutes intraoperatively for 2 hours.

In our study significantly more decrease in heart rate was observed after administration of loading dose of vecuronium compared to rocuronium especially at 2 and 3 minutes after administration of drug and this was observed prior to application of any stimulus like laryngoscopy or surgical incision which would affect hemodynamics. Hence the observed difference between these two drugs would be more indicative of effect of specific drug. But degree of fall was not significant from baseline in both the groups indicating that both drugs have shown good stability regarding heart rate but vecuronium having more tendencies to fall in heart rate.

In both the groups increase in heart rate was observed from baseline in response to laryngoscopy and intubation, with rocuronium showing significantly more response compared to vecuronium although this increase was only for short period. Intraoperatively more but non-significant decrease in heart rate from baseline was observed in V group (mean decrease-6.42%) as compared to R group (mean decrease-4.58%). Maximum percent decrease in heart rate in both group was less than 12%, indicating that both drugs have good haemodynamic stability as regards to heart rate with vecuronium showing more tendencies to decrease heart rate. J.B.Steven[11] studied haemodynamic effects of rocuronium and vecuronium. He found that heart rate decreased significantly in vecuronium group at all times after administration of drug while rocuronium group did not have significant effect on heart rate. Similarly study conducted by Eamon et al[14] in CABG patients showed significant decrease in heart rate in vecuronium group while rocuronium showed no significant change in heart rate. Study conducted by Harvey et al[15] (1999) in laparoscopic gynaecological procedures found that rocuronium had fewer episodes of bradycardia and rescue boluses of atropine required was less compared to vecuronium.

In present study, after induction and administration of vecuronium or rocuronium there was fall in systolic blood pressure, diastolic blood pressure and mean arterial pressure in both the groups when these parameters were recorded before laryngoscopy with slightly more but comparatively non-significant fall in these parameters in vecuronium group. After laryngoscopy both groups had significant rise in these parameters from their baseline but this rise was similar in both groups. Intraoperatively these parameters were comparable in both groups and no significant difference from baseline was observed in these parameters in both groups thereby showing good haemodynamic stability. G.D.Shorten et al[13] observed significant fall in both systolic and diastolic pressure after administration of rocuronium and vecuronium from their preoperative values. However when compared with post induction level there was no significant difference and the fall in both groups was similar.

Hence to conclude that vecuronium is associated with greater decrease in heart rate than rocuronium in clinical doses. No increase in heart rate was observed with rocuronium in doses used. In all other aspects (SBP, DBP, MAP) haemodynamic effects were similar in both groups with slightly greater but non-significant fall observed after administration of vecuronium group.

Thus understanding haemodynamic effects of muscle relaxants may help us in selection of most appropriate muscle relaxant in a given case after considering preoperative cardiac status, preoperative medications, anaesthetic drugs to be used, nature of surgery and desirable intraoperative hemodynamics.

Limitations of the study

No invasive haemodynamic monitoring technique was used.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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