Effect of Muscle Relaxants on Heart Rate, Arterial Pressure, Intubating Conditions and Onset of Neuromuscular Block in Patients Undergoing Valve Surgery

Sanjula Virmani, DA, DNB, Deepak K Tempe, MD, Vishnu Datt, DA, DNB, AS Tomar, MD, Amit Banerjee, MCh, Harpreet Singh Minhas, MCh, Sanjay Goel, MD
Department of Anaesthesiology & Intensive Care, G.B. Pant Hospital, New Delhi

Sixty six patients undergoing elective valve surgery were randomized to receive rocuronium bromide 0.6 mg/Kg (Group R, n=22), pancuronium bromide 0.1 mg/Kg (Group P, n=22) and vecuronium bromide 0.1 mg/Kg (Group V, n=22). Measurements of heart rate and arterial pressure (systolic, diastolic and mean) were noted at the following stages: 1) baseline when haemodynamics were stable for 2 minutes after induction of anaesthesia (2) one, (3) three, (4) five minutes after administration of muscle relaxants, (5) one, (6) three, and (7) five minutes after intubation. In group R, the heart rate decreased 5 min after injection of muscle relaxant from 93.9±21.3 to 82.4±20.7 beats/ min (p<0.001). However, it increased to 128.3 ± 25.8 beats/ min (p<0.001) following intubation and returned to baseline at 5 min after intubation. In group P, heart rate increased from 98.8±32.6 to 109.6±32.7 beats/min (p<0.001), 1 min after injection of pancuronium and this increase persisted throughout the study period. In group V, heart rate decreased from 99.9±22.3 to 83.8±19.6 beats/min (p<0.001) at 5 min after injection of the drug. It increased to 118.6 ± 22.4 beats/ min (p<0.001), 1 min after intubation and returned to baseline at 5 min after intubation. The decrease in heart rate in group R and V was accompanied by a significant decrease in systolic, diastolic and mean arterial pressures. In group P, only the systolic pressure decreased significantly at 5 min after injection of the drug. Intubation was accompanied by a significant increase in systolic, diastolic and mean arterial pressure in all the groups. Excellent intubation conditions (intubation score 3-4) were observed with all the three drugs, however, there were more number of patients in group P who showed diaphragmatic movement during intubation. Onset of action of muscle relaxant, was fastest with rocuronium (group R=132.7±0.3 sec, P=182.6±68.5 sec, V=144.8±46.1 sec, P<0.05, Group P vs Group R). To conclude, pancuronium causes significant increase in heart rate and should be preferred in patients with regurgitant lesions having slower baseline heart rate. Vecuronium and rocuronium decrease the heart rate and should be preferred in patients with faster baseline heart rate. In terms of intubating conditions rocuronium and vecuronium provide best conditions, but onset is faster with rocuronium. (Annals of Cardiac Anaesthesia 2006; 9: 37-43)

Key words: Muscle relaxants, Haemodynamics, Rocuronium, Pancuronium, Vecuronium
in patients undergoing coronary artery bypass graft (CABG) surgery\(^2,3\) and there is limited literature regarding its use in patients undergoing valve surgery in conjunction with morphine as the opioid. This study was undertaken to compare the HR and arterial pressure changes, intubating conditions and onset of neuromuscular block with rocuronium, pancuronium and vecuronium in patients undergoing valve surgery.

**Methods**

Sixty-six patients undergoing elective valvular heart surgery were prospectively studied after obtaining approval from the hospital ethics committee. Informed consent was obtained from each patient. Patients were randomised into three groups of 22 each. Group R received rocuronium bromide (0.6 mg/Kg, Esmeron, Infar India Ltd., Kolkata), group P received pancuronium bromide (0.1 mg/Kg, Pavulon, Infar India Ltd., Kolkata) and group V received vecuronium hydrochloride (0.1 mg/Kg, Norcuron, Infar India Ltd., Kolkata) as muscle relaxants. Patients with left ventricular ejection fraction <0.5, renal, hepatic, neuromuscular disorders, pregnancy, metabolic disorders, and heart failure were excluded from the study. Digoxin and furosemide were continued till the day of surgery. All patients were premedicated with morphine sulphate 0.2 mg/Kg and promethazine hydrochloride 25 mg, intramuscularly, 1 hour prior to surgery. In the operating theatre, 3 to 5 mg of morphine sulphate was given through a 23 gauge scalp vein needle and then the radial arterial and peripheral venous lines were inserted under local anaesthesia. Neuromuscular monitor (TOF Guard, Organon Teknika, N.V, Belgium) was connected via surface electrodes to assess the onset of neuromuscular block by train of four (TOF) stimulation of the ulnar nerve at the wrist. Anaesthesia was induced with morphine 25-30 mg and thiopentone 50-150 mg. Measurement of neuromuscular transmission was started immediately after induction of anaesthesia when a baseline automatic calibration of TOF Guard was done. Thereafter, baseline haemodynamic measurements (HR, systolic, diastolic, and mean arterial pressure were recorded when HR and arterial pressure were stable for 2 minutes. This was done with the intention of allowing the haemodynamic effects of induction agents to take place so that they did not interfere with the interpretation of haemodynamic effects of muscle relaxants. Muscle relaxant was then administered and haemodynamic measurements were recorded at 1, 3 and 5 min. Patient was intubated after 5 min, by a trained anaesthesiologist who was blinded to the muscle relaxant. The intubation conditions were rated, based on the state of vocal cords, coughing and ease of laryngoscopy, according to the modified version of scoring system described by Domaoal et al\(^4\) (Table 1). According to this scoring system, the lower score means better intubating condition. Haemodynamic measurements were recorded at 1, 3, and 5 minutes after intubation. Onset of action of muscle relaxant (in seconds) was recorded from the time of injection of muscle relaxant to, disappearance of response to all four stimuli in TOF Guard. Patients were administered nitrous oxide and oxygen using fractional inspired oxygen concentration of 0.5 throughout the study.

**Statistical Analysis**

Statistical analysis was done using SPSS 10.0 (SPSS Inc. Chicago) software. Pairwise comparisons were performed with a t-statistic corrected by Bonferroni test, Tukey’s test and Anova for multiple measurements. Data are expressed as mean ± S.D. Variables were considered significant, if p values were less than 0.05.

**Table 1. Intubation scoring system\(^4\)**

<table>
<thead>
<tr>
<th>Vocal Cords</th>
<th>Open</th>
<th>Moving</th>
<th>Closing</th>
<th>Closed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coughing</td>
<td>None</td>
<td>With diaphragm</td>
<td>Clear</td>
<td>Severe</td>
</tr>
<tr>
<td>Laryngoscopy</td>
<td>Easy</td>
<td>Fair</td>
<td>Difficult</td>
<td>Impossible</td>
</tr>
</tbody>
</table>

Points

|       | 1       | 2   | 3   | 4   |

Intubating conditions are rated as Excellent (score of 3-4), Good (score of 5-7), Poor (score of 8-10) and bad (score of 11-12)
Results

All patients belonged to younger age group and were comparable with respect to age, sex and weight (Table 2). The various types of valvular lesions and presence of atrial fibrillation are depicted in Table 3. A large proportion of patients suffered from mitral valve disease. Preoperatively, atrial fibrillation (AF) was present in 11 patients (3 in group R, 4 in group P, and 4 in group V). Table 4 shows the haemodynamic parameters observed at various stages in group R. The HR decreased from 93.9±21.3 to 82.4±20.7 beats/min (p<0.01), 5 min after injection of rocuronium. It increased to 128.3±25.8 beats/min (p<0.001) following intubation and returned to baseline at 5 min after intubation. The decrease in HR was accompanied by a significant decrease in systolic, diastolic, and mean arterial pressure before intubation. However, these parameters showed significant increase following intubation and followed the trend seen with HR. In summary the predominant haemodynamic effect in this group was negative chronotropic effect and a sympathetic response to intubation. The haemodynamic effects observed in group P are shown in Table 5. Pancuronium caused an increase in HR from 98.8±32.6 to 109.6±32.7 beats/min (p<0.001), 1 min after injection of the drug and this increase persisted throughout the study period with maximum increase to 140.8±35.0 beats/min, 1 min after intubation. Before intubation, only systolic arterial pressure showed a significant decrease, 5 min after injection of the drug (from 112.7±27.3 to 100.6±22.7 mm Hg, p<0.01), but after intubation, the systolic, diastolic and mean arterial pressures increased and remained so throughout the study period. In group V (Table 6), the haemodynamic changes observed, were more or less similar to those observed in group R i.e. a significant decrease in HR accompanied by a significant decrease in arterial pressure, 5 min after administration of the drug, and increase in these parameters after intubation. Statistical comparison between the groups showed that the baseline haemodynamic parameters in the three groups were not significantly different. Comparison of HR showed that pancuronium caused significantly more tachycardia compared with rocuronium and vecuronium at 3 and 5 min after injection of the drug, and 5 min after intubation. At 1 min after intubation the increase in HR was significantly more than vecuronium only (Fig. 1). The systolic arterial pressure (Fig. 2) showed that there were no differences in the groups and it decreased in all the three groups till 5 min after injection of the

Table 2. Showing age, weight and sex distribution in the three groups (mean ±SD)

<table>
<thead>
<tr>
<th></th>
<th>Group R (N=22)</th>
<th>Group P (N=22)</th>
<th>Group V (N=22)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>28.7±8.6</td>
<td>32.6±11.7</td>
<td>29.7±11.2</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>50.1±10.3</td>
<td>54.4±14.0</td>
<td>45.1±10.6</td>
</tr>
<tr>
<td>Sex M/F</td>
<td>10/10</td>
<td>15/5</td>
<td>8/12</td>
</tr>
<tr>
<td>P</td>
<td>NS</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3. Showing types of valvular lesions and presence of preoperative atrial fibrillation in the three groups

<table>
<thead>
<tr>
<th>Dominant lesion</th>
<th>Group R (N=22)</th>
<th>Group P (N=22)</th>
<th>Group V (N=22)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MS</td>
<td>2</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>MR</td>
<td>8</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>MS+MR</td>
<td>7</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>AS</td>
<td>1</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>AR</td>
<td>-</td>
<td>4</td>
<td>-</td>
</tr>
<tr>
<td>AS+AR</td>
<td>1</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>MS+MR+AS+AR</td>
<td>2</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>MR+AR</td>
<td>1</td>
<td>-</td>
<td>6</td>
</tr>
<tr>
<td>MS+AR</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>PRE-OP AF</td>
<td>3</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>P</td>
<td>NS</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 4. Showing haemodynamic parameters (mean±SD) observed at various stages in group R

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control</th>
<th>Min after relaxant</th>
<th>Min after intubation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>1</td>
<td>3</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>HR (beats/min)</td>
<td>93.9±21.3</td>
<td>94.2±23.8</td>
<td>82.4±20.7</td>
</tr>
<tr>
<td>SAP (mmHg)</td>
<td>123.3±26.7</td>
<td>124.5±29.6</td>
<td>109.6±22.7</td>
</tr>
<tr>
<td>DAP (mmHg)</td>
<td>62.00±11.2</td>
<td>63.8±12.8</td>
<td>56.7±13.7</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>81.4±11.3</td>
<td>82.5±14.4</td>
<td>73.7±13.8</td>
</tr>
<tr>
<td>1</td>
<td>3</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>3</td>
<td>5</td>
<td></td>
</tr>
</tbody>
</table>

* P<0.05, +P<0.01, $ P<0.001

HR: heart rate, SAP: systolic arterial pressure, DAP: diastolic arterial pressure, MAP: mean arterial pressure
muscle relaxant followed by an intubation response which tended to settle as time progressed. Similar trend was seen with diastolic arterial pressure (Fig. 3) except that at 1 and 3 min after intubation the diastolic arterial pressure was more in group R compared with group V (p<0.05). When the mean arterial pressure was compared between the groups (Fig. 4), similar changes were observed except that at 1 min after injection of the drug, group R had a higher mean arterial pressure as compared with group P.

Excellent intubation conditions were observed with all the 3 drugs. The mean score in group P was highest, but not statistically significant (Table 7) and there were more number of patients in this group who showed diaphragmatic movement during intubation (2 patients in group R, 5 in group P and 1 in group V, p=NS).

Table 5. Showing haemodynamic parameters (means±SD) observed at various stages in group P

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control</th>
<th>Min after relaxant</th>
<th>Min after intubation</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (beats/min)</td>
<td>98.8±32.6</td>
<td>109.6±32.7*</td>
<td>113.9±36.8*</td>
</tr>
<tr>
<td>SAP (mmHg)</td>
<td>112.7±27.3</td>
<td>110.6±28.7</td>
<td>100.6±22.7*</td>
</tr>
<tr>
<td>DAP (mmHg)</td>
<td>57.4±9.4</td>
<td>57.1±11.1</td>
<td>52.4±11.9</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>73.3±12.0</td>
<td>72.3±10.9</td>
<td>68.1±12.8</td>
</tr>
</tbody>
</table>

*p<0.05 , +P<0.01, $P<0.001
HR: heart rate, SAP: systolic arterial pressure, DAP: diastolic arterial pressure, MAP: mean arterial pressure

Table 6. Showing haemodynamic parameters (mean±SD) observed at various stages in group V

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control</th>
<th>Min after relaxant</th>
<th>Min after intubation</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (beats/min)</td>
<td>99.9±22.3</td>
<td>97.7±22.4</td>
<td>83.8±19.6*</td>
</tr>
<tr>
<td>SAP (mmHg)</td>
<td>112.3±20.7</td>
<td>110.8±24.4</td>
<td>99.7±22.2*</td>
</tr>
<tr>
<td>DAP (mmHg)</td>
<td>57.4±10.5</td>
<td>55.8±11.6</td>
<td>51.2±10.4</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>75.8±10.1</td>
<td>73.4±12.5</td>
<td>68.1±10.7*</td>
</tr>
</tbody>
</table>

*p<0.05 , +P<0.01, $P<0.001
HR: heart rate, SAP: systolic arterial pressure, DAP: diastolic arterial pressure, MAP: mean arterial pressure

Fig. 1. Changes in heart rate at various stages in the three groups.

Fig. 2. Changes in systolic arterial pressure at various stages in the three groups.

Fig. 3. Changes in diastolic arterial pressure at various stages in the three groups.

Fig. 4. Changes in mean arterial pressure at various stages in the three groups.
Onset of action of muscle relaxant (Table 8) was fastest with rocuronium (132.7±70.3 seconds) and was significantly quicker when compared with pancuronium (182.6±68.5 seconds, p<0.05).

Table 7. Showing intubation scores in the three groups (mean ± S.D) according to the intubation scoring system*

<table>
<thead>
<tr>
<th>Group</th>
<th>Intubation Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group R</td>
<td>3.6±1.1</td>
</tr>
<tr>
<td>Group P</td>
<td>4.1±0.9</td>
</tr>
<tr>
<td>Group V</td>
<td>3.4±0.6</td>
</tr>
<tr>
<td>P=NS</td>
<td></td>
</tr>
</tbody>
</table>

Table 8. Showing onset of action of muscle relaxants

<table>
<thead>
<tr>
<th>Group</th>
<th>Onset of action (in seconds)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group R</td>
<td>132.7±70.3</td>
</tr>
<tr>
<td>Group P</td>
<td>182.6±68.5</td>
</tr>
<tr>
<td>Group V</td>
<td>144.8±46.1</td>
</tr>
<tr>
<td>P&lt;0.05, Group R vs P</td>
<td></td>
</tr>
</tbody>
</table>

Discussion

In this study rocuronium was compared with pancuronium and vecuronium in patients undergoing valve surgery anaesthetised with modest doses of morphine. Pancuronium caused significant tachycardia 1 min after injection. This effect persisted throughout the study period with maximum increase to 140.8±35 beats/min, 1 min after intubation, an effect which is well described in patients with VHD.5-7 Rocuronium and vecuronium decreased the HR, 1 min after injection of the drug and this decrease became significant after 5 min. The decrease, however, was not clinically significant and hence did not require any treatment. Although the decrease in HR by vecuronium is well documented in patients with VHD,6-8 the significant decrease in HR observed with rocuronium is rather unusual. A few studies have shown slight increase (5 to 7%) in HR3,9 while others9,10 have reported no change in HR with rocuronium in patients undergoing CABG under fentanyl anaesthesia. Borgeat and colleagues11,12 have reported that increase in HR with rocuronium is due to pain on injection. In none of these studies, rocuronium was used with morphine in patients undergoing valve surgery. The absence of vagolytic effect of rocuronium in this study maybe related to the use of 3×ED95 dose of rocuronium (that produces minimal cardiovascular effects both in healthy patients15-16 and in those with cardiovascular disease),2,17 anaesthetized with modest dose of morphine (that is known to cause stimulation of central vagal nucleus).18 The HR increased in all the three groups after intubation. Intergroup comparison showed that the increase in HR caused by pancuronium was significantly more when compared with other two drugs, while there was no significant difference between rocuronium and vecuronium. The BP decreased in all the three groups at 5 min after administration of muscle relaxant.

Onset of action of muscle relaxant was taken as the time from the end of injection to the maximum effect. The mean onset time was 132.7±70.3, 144.8±46.1 and 182.6±68.5 seconds for rocuronium, vecuronium and pancuronium respectively. There is a wide variation in the onset time reported by various authors. An onset time of 155±85,19
213±17,20 204±72,15 65.5±12,12 and 93±25 seconds,21
for rocuronium; 216±96,15 170±70,19 and 124±20.1
seconds14 for vecuronium; and 3.5 min22 and
180±75 seconds18 for pancuronium has been
reported. This variation in time may be related to
the dose of the muscle relaxant and the definition
of onset time. In addition, these reports are in
noncardiac patients so that differences in
pharmacodynamics may have been a factor. It is
known that patients with low cardiac output
require a longer time before a twitch depression of
>90% is obtained.23

All the three drugs provided excellent intubation
scores (3-4 on the Domaoal scoring system).
However there were more number of patients in
group P (5 in group P, 2 in group R and 1 in group
V), who showed diaphragmatic movement during
intubation. Wierda et al15 have reported a mean
score of 3.7 with rocuronium which is similar to
that seen in this study (group R = 3.0±1.1). Mehta
et al1 have reported least incidence of
diaphragmatic movement with pancuronium as
compared with atracurium and vecuronium. The
recommended intubating doses of muscle
relaxants25 have been used in the present study and
we are unable to explain this difference in the
incidence of diaphragmatic movement.

VHD causes alteration in cardiac loading
conditions and ventricular contractility. Thus,
during anaesthetic induction it is wise to choose
suitable vasoactive drugs and a muscle relaxant
to match the cardiovascular needs of the patient.
Anaesthetic agents causing tachycardia or
profound vasodilatation should be avoided in
mitral stenosis, while in mitral regurgitation, to
maximize the forward flow and reduce the
regurgitant flow, a slight increase in HR is
preferable. In aortic stenosis stroke volume is
limited and cardiac output (CO) is rate dependent,
thus bradycardia can cause a decrease in CO. A
faster HR is therefore desirable. Maintenance of
sinus rhythm is also important in aortic stenosis,
as ventricular filling depends upon the atrial kick.
In aortic regurgitation vasodilation and increased
HR should be the goals of safe anaesthesia because
bradycardia can cause left ventricular distension
which is dangerous in patients with severely
hypertrophied hearts. However, mixed and
multiple valvular lesions occur very commonly in
patients with RHD and combined stenotic and
regurgitant lesions impose extra burden on the
heart. Thus, it is always useful to take into
consideration the basal HR of the patient before
choosing the muscle relaxant.5

In conclusion, pancuronium that caused
significant tachycardia and sympathetic response
to intubation (which in cardiac anaesthesia has
earlier been implicated in episodes of myocardial
ischaemia24) should be used in regurgitant lesions
to maximize the forward flow, in patients with
slower basal HRs. Vecuronium and rocuronium
that decrease the HR, should be the preferred drugs
in patients having faster baseline HRs. In terms of
intubating conditions, rocuronium and
vecuronium provide best conditions but onset is
quicker with rocuronium.

References

1. Wierda JM, Kleef UW, Lambalk LM, et al. The
pharmacodynamics and pharmacokinetics of Org 9426,
a new non-depolarising neuromuscular blocking agent
in patients anaesthetized with nitrous oxide, halothane
Comparison of haemodynamic effects of rocuronium
bromide with those of vecuronium in patients undergoing
effects of rocuronium during fentanyl anaesthesia:
comparison with vecuronium. Can J Anaesth 1993; 40:
703-708
4. Domaoal AM, Weniger FC, Wolfson B. “Precurarization”
using pancuronium. Anesth Analg 1975; 54: 71-75
relaxants on heart rate and blood pressure in patients
14: 147-152
effects of vecuronium and pancuronium in patients
undergoing elective closed mitral valvotomy. Indian J Med
Res 1991; 94: 211-216
7. Sethna DH, Starr NJ, Estafanos FG. Cardiovascular
effects of nondepolarizing neuromuscular blockers in
patients with aortic valve disease. Can J Anaesth 1987; 34:
582-588
16. Wierda JM, Schuringa M, vanden Broek L. Cardiovascular effects of an intubating dose of rocuronium 0.6 mg/kg in anaesthetized patients, paralysed with vecuronium. *Br J Anaesth* 1997; 78: 586-587