

# A Study of Biochemical Changes of Rocuronium Bromide and other Muscle Relaxants in Cardiac Surgery

Sanjay Kumar Gupta<sup>1</sup>, Jitendra Kumar<sup>2</sup>, Reena Singh<sup>3</sup>, Sajid Khan<sup>4</sup>, Shushil Kumar<sup>5</sup>

## ABSTRACT

**Introduction:** Neuromuscular blockers like Rocuronium bromide can impair respiratory functions during general anaesthesia. Therefore aim of present study was to find out the biochemical changes of Rocuronium bromide and other muscle relaxant in cardiac surgery.

**Material and Methods:** Present study was carried out on sixty (60) patients of different age groups from both sexes scheduled for various cardiac surgical procedures at L.P.S. Institute of Cardiology, GSVM medical college Kanpur during the period of August 1998 to August 1999. Patients were classified in 3 equal groups. Muscle relaxants were given according to the group and biochemical parameters like PCO<sub>2</sub>, PO<sub>2</sub>, pH etc. were recorded carefully at the interval of two, five and ten minutes.

**Results:** No statistically significant changes were observed in PCO<sub>2</sub>, pH, Na<sup>+</sup>, K<sup>+</sup> at 2 minutes, 5 minutes and 10 minutes after the administration of all three drugs ( $P > 0.05$ ) compared with control values. Statistically Significant changes in PO<sub>2</sub> and O<sub>2</sub> saturation was observed at 2 minutes, 5 minutes and 10 minutes after the administration of Pancuronium ( $P < 0.05$ ).

**Conclusion:** Rocuronium bromide is safer in cardiac surgery as compared to other muscle relaxants.

**Keywords:** Anaesthesia, Biochemical, Cardiac Surgery, Pancuronium, PCO<sub>2</sub>

## INTRODUCTION

Various synthetic non-depolarizing muscle relaxants e.g. gallamine triethiodate, pancuronium bromide, vecuronium, bromide, atracurium besylate have been used as an integral part of modern anaesthesia. Main objective of muscle relaxant is to facilitate endotracheal intubation and to provide surgical relaxation.<sup>1-3</sup> Performance of endotracheal intubation depends upon various factors i.e. depth of anaesthesia, muscle relaxation degree and skill of anaesthesiologist.<sup>2</sup> Type of surgery & muscle relaxant's duration are critical factors for selection of correct muscle relaxant for successful tracheal intubation.<sup>4</sup>

Due to high risk of respiratory function impairment induced by postoperative residual curarization (PORC), attention has been paid to PORC after general anaesthesia involving neuromuscular blockers.<sup>5-7</sup> Recently, it has been suggested that the traditional recovery criterion of "train-of-four (TOFR)  $\geq 0.9$ " should be used as a standard for complete recovery instead of "TOFR = 0.7."<sup>8</sup> Many factors like hypothermia, inhalational anaesthetics and acid-base imbalance relate to the changing pharmacodynamics of muscle relaxants, which may prolong action or delay recovery, increasing the risk of

PORC.<sup>9-11</sup>

CO<sub>2</sub> retention frequently occurs during or after surgeries requiring general anaesthesia and common in pneumoperitoneal laparoscopic surgery<sup>12, 13</sup> or one-lung ventilation in open chest operations<sup>14</sup>. Therefore, high levels of CO<sub>2</sub> have influence on recovery from muscle relaxation. Various studies have demonstrated interactions between neuromuscular blockers and respiratory acidosis; including pancuronium, atracurium, and Vecuronium.<sup>15-17</sup> Thus aim of present study is to evaluate biochemical parameters like PCO<sub>2</sub>, PO<sub>2</sub>, pH etc after rocuronium bromide and other muscle relaxant administration in cardiac surgery.

## MATERIAL AND METHOD

After obtaining Institutional Ethical Committee clearance and written informed consent for surgery and general anaesthesia, present study was carried out on sixty (60) patients of different age groups from both sexes scheduled for various cardiac surgical procedures at L.P.S. Institute of Cardiology, GSVM medical college Kanpur during the period of August 1998 to August 1999. Patients with pre-existing neuromuscular disorders like myasthenia gravis or history of drug intake like streptomycin, neomycin etc. known to influence neuromuscular transmission were excluded from the study. Patients were classified into three groups as follows-

Group A: Pancuronium bromide (20 patients)

Group B: Vecuronium bromide (20 patients)

Group C: Rocuronium bromide (20 patients)

Various biochemical parameters like arterial blood gas, pH, PO<sub>2</sub>, Pco<sub>2</sub>, base excess, O<sub>2</sub> saturation and electrolytes like

<sup>1</sup>Assistant Professor, Dept of Anesthesia, Prasad Institute of Medical Sciences, Lucknow (U.P.), <sup>2</sup>Assistant Professor, Department of Anaesthesia, Government Medical College, Banda (U.P.), <sup>3</sup>Associate Professor, Department of Medicine, Government Medical College, Banda (U.P.), <sup>4</sup>Resident, Department of Dentistry, Government Medical College, Banda (U.P.), <sup>5</sup>Assistant Professor, Department of Anaesthesia, Government Medical College, Banda (U.P.), India

**Corresponding author:** Jitendra Kumar, Assistant Professor, Department of Anaesthesia, Government Medical College, Banda (U.P.), India

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Na<sup>+</sup>&K<sup>+</sup> were studied and analysed. Blood gas analysis and electrolytes were checked by blood gas module by EG0-7 (i-stat) method (HP monitor). Pre-anaesthetic assessment and routine investigations were done prior to surgery. Patients were graded according to the American society of anaesthesiologist (ASA). Patients of ASA class I, II and III were included in this study. All patients were premedicated with intramuscular injection of morphine (0.1–0.2 mg/kg) and injection promethazine (25 mg), 45 minute before induction in the pre-operative room.

All patients were pre oxygenated for 3-5 minutes and induced with 3-5 mg/kg of IV injection of thiopentone sodium and intubation was achieved with 2 mg/kg of suxamethonium. A central venous triple lumen catheter (Arrow) & radial arterial line (20 gohmeda) were put in the right internal jugular vein & in radial artery respectively immediately after induction. Then after putting CVP catheter and radial line, all the parameters described above were taken immediately and recorded. Then patients were given muscle relaxant according to the group and above mentioned parameters were recorded carefully at the interval of two, five and ten minutes.

After endotracheal intubation patients were connected with anaesthetic ventilator (Ohmeda 7800) and anaesthesia was maintained with 50% O<sub>2</sub> and 50% N<sub>2</sub>O with intermittent positive pressure ventilation. Volatile inhalational anaesthetic

agents were not used for maintenance of anaesthesia. Reversal of anaesthesia was not done at the end of surgery in open heart surgery cases & all the patients were kept on ventilator post operatively and gradually weaned off accordingly. All closed heart surgery patients were reversed & extubated on table.

## STATISTICAL ANALYSIS

Statistical comparisons were made by using 'T' test. Control values were compared with the value at 2 min. after muscle relaxant given, 5 min. after muscle relaxant given & 10 min after muscle relaxant given for PCO<sub>2</sub>, PO<sub>2</sub>, O<sub>2</sub> saturation, pH, Na<sup>+</sup>, K<sup>+</sup>.

## RESULTS

Table 1 shows that out of 60 patients, 35 (58.33%) were males and 25 (41.67%) were female. It is also evident that the maximum patients (31.67%) belonged to 30-40 years age group where minimum patients (3.34%) were of 10-20 years age group. The maximum patients (26.67%) were operated for mitral valve replacement.

Table 2 represents biochemical parameter response to pancuronium bromide administration. No statistically significant changes were observed in PCO<sub>2</sub>, pH, Na<sup>+</sup> and K<sup>+</sup> at 2 minutes, 5 minutes and 10 minutes after the administration of drug ( $P > 0.05$ ) compared with control values. Significant

Age group (Yr)	Group A		Group B		Group C		Total No.	%
	Male	Female	Male	Female	Male	Female		
10-20	1	0	0	0	0	1	2	3.34
20-30	2	1	3	1	2	0	9	15.0
30-40	5	1	4	2	3	4	19	31.67
40-50	3	3	2	2	3	4	17	28.33
50-60	1	2	3	1	0	1	8	13.33
60-70	0	1	2	0	1	1	5	8.33
Total	12	8	14	6	9	11	60	100.0

**Table-1:** Distribution of cases according to age and sex

Parameter	0 min	2 min	5 min	10 min
Po <sub>2</sub>	196.50±22.71	212.65±9.92*	240.0±13.07*	255.53±13.94*
PCo <sub>2</sub>	37.46±3.85	37.35±3.97	38.57±5.40	38.63±4.97
pH	7.40±0.039	7.39±0.066	7.41±6.14	7.40±0.56
O <sub>2</sub> saturation	98.92±1.34	99.10±1.05*	99.81±0.199*	99.72±0.45*
Na <sup>+</sup>	136.10± 4.05	136.4±4.12	137.15±4.09	137.15±4.06
K <sup>+</sup>	3.39±0.05	3.96±0.50	3.93±0.49	3.89±0.47

\* Represents the p value <0.05.

**Table-2:** Biochemical Parameters Response to Pancuronium Bromide Administration

Parameter	0 min	2 min	5 min	10 min
Po <sub>2</sub>	200.26±12.92	203.3±23.98*	245.24±24.17*	264.59±49.35*
PCo <sub>2</sub>	36.77±4.15	36.73±4.93	38.33±14.30	39.88±1.18
pH	7.36±0.05	7.4±0.044	7.47±0.170	7.40±0.056
O <sub>2</sub> saturation	99.00±1.12*	98.64±1.39*	99.83±0.255*	99.55±0.52*
Na <sup>+</sup>	136.1±4.88	136.35±5.06	135.9±5.2	136.9±4.77
K <sup>+</sup>	4.19±1.41	4.06±.598	4.025±0.067	3.96±0.58

\* Represents the p value <0.05.

**Table-3:** Biochemical Parameters Response to Vecuronium Bromide Administration

Parameter	0 min	2 min	5 min	10 min
Po <sub>2</sub>	184.78±32.92*	213.19±41.42*	243.57±38.26*	252.25±40.38*
PCo <sub>2</sub>	36.31±2.73	37.78±2.67	37.67±5.96	38.28±4.48
pH	7.37±0.076	7.36±0.071	7.42±0.058	7.41±0.063
O <sub>2</sub> saturation	119.02±0.799*	98.68±1.32*	99.42±0.79*	99.57±0.69*
Na <sup>+</sup>	138.25±3.43	139.09±2.78	139±2.22	138.65±2.49
K <sup>+</sup>	3.92±0.39	3.93±0.384	4.08±0.28	3.99±0.28

\* Represents the p value <0.05.

**Table-4:** Biochemical Parameters Response to Rocuronium Bromide Administration

increase in Po<sub>2</sub> and O<sub>2</sub> saturation were observed at 2 minutes, 5 minutes and 10 minutes after the administration of drug ( $P < 0.05$ ).

Table 3 represents biochemical parameters response to vecuronium bromide administration. No statistically significant changes were observed in PCO<sub>2</sub>, pH, Na<sup>+</sup> and K<sup>+</sup> at 2 minutes, 5 minutes and 10 minutes after the administration of drug ( $P > 0.05$ ) compared with control values. Significant increase in Po<sub>2</sub> and O<sub>2</sub> saturation were observed at 2 minutes, 5 minutes and 10 minutes after the administration of drug ( $P < 0.05$ ).

Table 4 represents biochemical parameters response to rocuronium bromide administration. No statistically significant changes were observed in PCO<sub>2</sub>, pH, Na<sup>+</sup> and K<sup>+</sup> at 2 minutes, 5 minutes and 10 minutes after the administration of drug ( $P > 0.05$ ) compared with control values. Significant increase in Po<sub>2</sub> and O<sub>2</sub> saturation were observed at 2 minutes, 5 minutes and 10 minutes after the administration of drug ( $P < 0.05$ ).

## DISCUSSION

The present study was carried out on 60 patients of different age groups & sex who underwent major cardiac surgical procedure for different pathological conditions at LPS institute of GSVM Medical College Kanpur.

Dose of muscle relaxants depends upon physical built of patients, the normality of the neuromuscular transmission, the presence or absence of certain diseases affecting metabolism and excretion of drugs. Same standard premedication was used in all cases to avoid the influence on the dosages and action of muscle relaxant drug.

Nitrous oxide should have similar effect in all patients, therefore, has no effect on results of our study. Inhalation agents having myocardial depressant effect have not been used in this study. All patients were included under American society of Anaesthesiologists (ASA) class I, II, III. All cases were screened pre-operatively & thorough clinical examinations were done.

O<sub>2</sub> saturation and PO<sub>2</sub> in arterial blood gas were showing highly significant change in all groups. After endotracheal intubation it is very much expected an increase in PO<sub>2</sub>.

There is no significant change in Na<sup>+</sup> & K<sup>+</sup> after giving muscle relaxant so far as the results of serum Na<sup>+</sup> & K<sup>+</sup> after administration of Pancuronium, Vecuronium & Rocuronium, are concerned. It has not been possible to compare statistically due to lack of available literature. However the amount chosen as control in our study was adequate and has not resulted in

any untoward effect. Study done by Teng L et al.<sup>18</sup> indicated that there was significantly prolonged spontaneous recovery in high PaCO<sub>2</sub> level compared to normal or low level PaCO<sub>2</sub> from rocuronium-induced neuromuscular blockade. Mean times of spontaneous recovery index and recovery time of TOFR to 0.9 was increased by three minutes and five minutes respectively with PaCO<sub>2</sub> increased in 6 to 8 mmHg increments. Both recovery index and recovery time could be accelerated by small doses of neostigmine under any level of PaCO<sub>2</sub>, but the delay of both did not achieve statistical significance till increase of PaCO<sub>2</sub> exceeded 15 mmHg under the condition of neostigmine reversal. Above study concluded that PaCO<sub>2</sub> had an significant effect on recovery of rocuronium induced neuromuscular blockade & on its reversal, as soon as it reached high enough levels.

Various studies have demonstrated the effect of acid-base balance on the pharmacokinetics or pharmacodynamics of muscle relaxants, but varying conclusions have been shown. Study done by Platt et al.<sup>19</sup> observed that respiratory alkalosis significantly shortened the duration of atracurium action. Various other studies observed the effect of hypocapnia and hypercapnia on twitch response in pancuronium-induced neuromuscular blockade reversed by neostigmine 35 µg/kg. Wirtavuori K et al.<sup>20</sup> found that maximal depressions of twitch response were altered significantly by both hypercapnia (up to 75%) and hypocapnia, while twitch response recovery up to 50% was not changed by either hypercapnia or hypocapnia. Study done by Yamauchi M et al.<sup>21</sup> observed that the duration of action and the rate of recovery index of vecuronium were delayed by acidosis resulting from hypercapnia. Gencarelli et al.<sup>22</sup> found that the recovery index of vecuronium-induced neuromuscular blockade in humans was not significantly changed by hyperventilation-induced hypocapnia.

Study done by Teng L et al.<sup>18</sup> confirmed a linear relationship between PaCO<sub>2</sub> and spontaneous recovery times from Rocuronium. It supported that there is an effect of CO<sub>2</sub> retention on recovery from muscle relaxation, especially for rocuronium-PaCO<sub>2</sub> interaction. Rocuronium is one of the muscle relaxants of choice in clinical practice because of its fast onset, easy titration, and short duration. Therefore, the current study illuminates the interaction between carbon dioxide blood levels and rocuronium, helping us to better evaluate, determine and deal with recovery from neuromuscular blockade.

The maximum and minimum values of PaCO<sub>2</sub> were set for patient safety while differing as widely as possible. Recovery times of the hypoventilation and hyperventilation groups

were no different than those of the normo ventilation group after neuromuscular blockade was reversed by small doses of neostigmine. This suggests the following hypothesis: if the level of PaCO<sub>2</sub> is intentionally made higher, the influence on recovery times may be even greater, and statistically significant differences may be found for the comparisons between normoventilation and hyper or hypo- ventilation. However, if much larger doses of neostigmine are used, the recovery times may be even more accelerated and differences may be more difficult to achieve between the groups. It has been reported that for PaCO<sub>2</sub> ≤ 80 mm Hg and pH ≥ 7.15, the adverse physiological effects of hypercapnia were often reversible.<sup>23</sup> Moreover; permissive hypercapnia has recently been regarded as beneficial for the treatment of respiratory diseases.<sup>24</sup>

## CONCLUSION

From result of present study, we conclude that Rocuronium bromide has no significant change in pH value like Vecuronium & Pancuronium. All three muscle relaxant groups have no significant change in PCO<sub>2</sub> level. Rocuronium bromide has significant change in PO<sub>2</sub> and O<sub>2</sub> saturation level like Vecuronium & Pancuronium. All three muscle relaxant groups have no significant effect on serum Na<sup>+</sup> level.

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