

## Effect of Saline Flush and Hand Elevation on the Onset, Time and Duration of the Action of Rocuronium

*Manar Adnan Habash, Sanaa Fareed Qassim*

### **ABSTRACT:**

#### **BACKGROUND:**

Nondepolarizing neuromuscular blocking drugs (NMBDs) were developed as alternatives to Succinylcholine due to its serious side effects. Rocuronium bromide has been suggested as the drug of choice when Succinylcholine is contraindicated. Shortening the onset time of NMBDs is important in some situations, which can be achieved by several techniques as the priming principle.

#### **OBJECTIVE:**

To evaluate the effect of fluid (normal saline) flush after Rocuronium bolus on the onset and duration of action.

#### **PATIENTS AND METHODS:**

Sixty patients were divided randomly into two groups; each group had 30 patients: group (A) and group (B). All of them have undergone surgical operations under general anesthesia. Rocuronium without normal saline was received in induction by 30 patients (Group A), while Rocuronium followed by 20 ml normal saline flush and hand elevation were received in induction by the other 30 patients (Group B). A peripheral nerve stimulator was used to measure a train-of-four (TOF) stimulation. The time from the disappearance of T1 until the appearance of T3 is the duration of the action of Rocuronium.

#### **RESULTS:**

In this study, means of time of onset were significantly higher in Group A than that in Group B (61.12 versus 44.41 sec,  $P=0.001$ ), and duration of action was higher in Group B than that in Group A but statistically not significant (40.87 versus 34.61 mins,  $P=0.063$ ).

#### **CONCLUSION:**

A 20 ml saline flush and hand elevation immediately after administering a Rocuronium bolus of (0.6 mg/kg) decreased the onset time but did not significantly increase the recovery phase of Rocuronium. Therefore, we recommend to use 20 ml Normal Saline flush and hand elevation after Rocuronium injection as a safe method to get rapid onset for intubation especially when Suxamethonium is contraindicated.

**KEYWORDS:** General Anesthesia, Succinylcholine, Non-depolarizing neuromuscular blocking drugs, Rocuronium, Normal Saline, Hand Elevation

### **INTRODUCTION:**

Over the past decade, the practice of rapid sequence induction in anesthesia has evolved with the availability of new drugs, equipment, and knowledge. This technique is employed daily during emergency surgery. A classical rapid sequence induction has employed thiopental as an induction agent and succinylcholine for neuromuscular block. Succinylcholine was once considered to be the most appropriate muscle relaxant to facilitate the endotracheal intubation during induction of anesthesia.

The continued popularity of succinylcholine is due to its rapid onset of action (30-60 sec.) and short duration of action (typically less than 10 min.)<sup>1</sup> However, it can also cause serious side effects<sup>2</sup>. Several induction agents and several alternatives to succinylcholine are used by many anaesthetists due to its serious side effects that may include hyperkalemia, severe bradycardia after a second dose, increase in intracranial pressure<sup>3,4,5,6</sup> malignant hyperthermia, and prolonged paralysis (atypical pseudocholinesterase).<sup>1</sup> Several studies have been conducted to develop new non-depolarizing neuromuscular blocking drugs (NMBDs) with an onset of action similar to that of succinylcholine<sup>7,8</sup>.

## ACTION ROCURONIUM

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They block the binding of neurotransmitters to a subunit of the nicotinic acetylcholine receptor (nAChR) at the neuromuscular junction of the motor neurons of skeletal muscle<sup>9</sup> preventing acetylcholine from reaching one or both subunits of the receptor.

Rocuronium bromide has been suggested as the drug of choice when Suxamethonium is contraindicated. It produces better intubating conditions in a shorter time.<sup>10</sup>

Shortening the onset time of NMBDs is important in some situations. Several protocols have been proposed for this purpose, including the use of the priming principle or timing principle, and administration of large doses<sup>11,12,13</sup>

The onset time of non-depolarizing neuromuscular blocking drugs (NMBDs) depends partly on factors such as circulation time and muscle blood flow.<sup>14</sup>The site of administration should be elevated above the heart or a catheter with a large inner diameter should be used to rapidly achieve high target concentration of non-depolarizing neuromuscular blocking drugs(NMBDs)<sup>15</sup>.

A peripheral nerve stimulator (PNS) is the most widely used monitor for assessment of the level of neuromuscular block (NMB) in the clinical environment.<sup>16,17</sup>

We aim in our study to evaluate the effect of fluid (normal saline) flush after the Rocuronium bolus on the onset and duration of action.

### **MATERIALS AND METHODS:**

This study was performed in Baghdad Teaching Hospital and Imamein Kadhimin medical city. After taking written consent from them, 60 adult patients were scheduled for elective surgery requiring general anesthesia in this study.

The inclusion criteria included: both genders, ages 12 to 70 years, any operation needs GA and intubation, and an ASA physical status I-II. Exclusion Criteria included Patients allergic to study drugs, Patients receiving treatment that affected on neuromuscular function, and pregnant women.

The sixty patients were divided randomly into two groups; each group had 30 patients: group (A) and group (B).

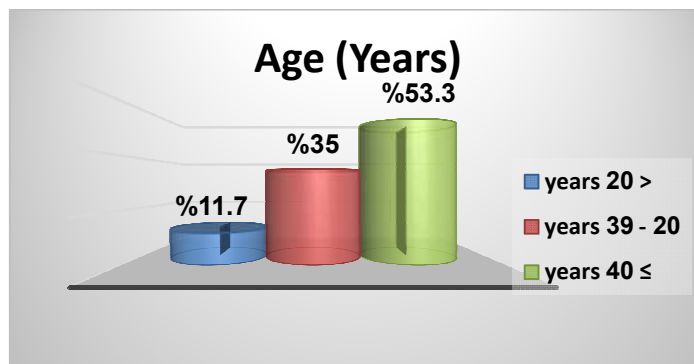
All patients had a 20-gauge peripheral venous catheter which was inserted into a large hand vein and connected to 2, 3-way stopcocks. The first 3-way stopcock was directly connected to the IV catheter and was used for administration Rocuronium, and the second 3-way was directly connected to the first stopcock and was used for administration flush normal saline. Routine monitoring was started once patients reached the surgical theater including electrocardiography, noninvasive arterial blood pressure, and pulse oximetry. Neuromuscular blocked was evaluated by an electromyography at the adductor pollicis muscle with train-of-four (TOF) stimulation for the other hand.

All patients had pre-oxygenation for 5 min. with 100%O<sub>2</sub>, premedication by Midazolam (0.03mg/kg) , Propofol anesthetizing dose of 1.5-2.5mg/kg, Sevoflurane with face mask 4%, Rocuronium ( 0.6mg/kg) in 10 mL of Normal Saline (after loss of eyelash reflex) for group (A). While for the second group (B), the dose of Rocuronium was followed by 20ml Saline flush immediately with hand elevation for one minute , then for both groups a nerve stimulator ( train-of-four (TOF) stimulation) was used at the adductor pollicis muscle every 20 seconds from end of administration of Rocuronium and Saline. The arm temperature was monitored using a surface probe, and kept at or above 32 °C using a heating blanket, until the disappearance of T4, T3 (time of onset of action), then intubation was done after the disappearance of T1 and inhalation anesthesia was continued after 10 min. from the disappearance of T1, TOF stimulation (every 10min.) until appearance of T3. The time from the disappearance T1 until appearance of T3 is duration of action. Both groups had the same type of fluid according to patients' weight and fasting hours, blood pressure was measured every 5 min.

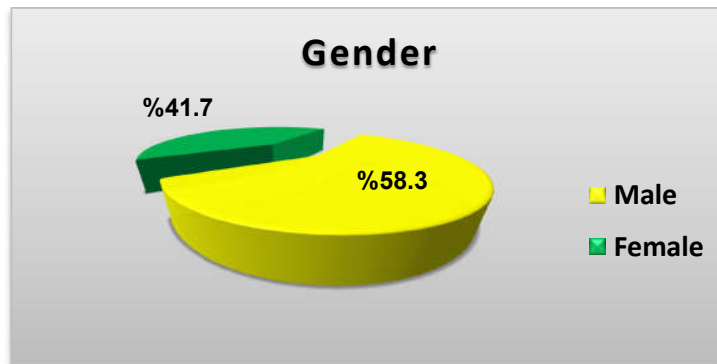
**RESULTS:**

The total number of patients in this study was 60. All of them have undergone surgical operations under general anesthesia. Rocuronium without normal saline was received in induction by 30 patients (Group A), while Rocuronium followed by 20 ml normal saline flush and hand elevation were received in induction by the other 30 patients (Group B). The distribution of study patients by general characteristics is shown in figure (1.1 and 1.2).

Study patient's age was ranging from 12 to 68 years with a mean of 41.88 years and standard deviation (SD) of  $\pm 17.05$  years. The highest proportion of study patients was aged  $\geq 40$  years (53.3%). Regarding gender, proportion of males was higher than females (58.3% versus 41.7%) with a male to female ratio of 1.39:1. The BMI was normal in all patients .



**Figure 1.1: Distribution of study patients by age**



**Figure 1.2: Distribution of study patients by gender**

When comparing between the study groups in relation to the general characteristics of study patients, we noticed that there were no

significant differences ( $P \geq 0.05$ ) in age, BMI, and gender between study groups as shown in table (1.1) and (1.2).

Table 1.1: Comparison between study groups in age and BMI.

Variable	Study Group		P- Value
	Group A Mean $\pm$ SD	Group B Mean $\pm$ SD	
Age (Years)	40.36 $\pm$ 16.65	43.4 $\pm$ 17.58	<b>0.496</b>
BMI Level (kg/m <sup>2</sup> )	23.62 $\pm$ 6.2	22.83 $\pm$ 5.21	<b>0.492</b>

Table 1.2: Comparison between study groups in gender

Variable	Study Group		Total (%) n= 60	P- Value
	GroupA n= 30	GroupB n= 30		
<b>Gender</b>				
Male	20 (66.7)	15 (50.0)	35 (58.3)	<b>0.19</b>
Female	10 (33.3)	15 (50.0)	25 (41.7)	

**Clinical parameters****In Group A**

The comparison between induction and post induction MAP and pulse rate in group A is shown in table (1.3).

In this study, the means of MAP and pulse rate had no statistical differences in post induction compared to those at induction ( $P \geq 0.05$ ).

Table 1.3: Comparison in mean between induction and post induction for clinical parameters in group A

Variable	Group(A) Mean $\pm$ SD	P- Value
<b>Mean Arterial Pressure (MAP)</b>		
Induction	92.73 $\pm$ 9.56	<b>0.79</b>
Post Induction	93.2 $\pm$ 8.05	
<b>Pulse Rate (beat/min) (PR)</b>		
Induction	95.08 $\pm$ 12.22	<b>0.277</b>
Post Induction	98.0 $\pm$ 7.43	

**In Group B**

The comparison between induction and post induction MAP and pulse rate in group B is shown in table (1.4). In this study, the means of

MAP and pulse rate had no statistical difference in post induction compared to those at induction ( $P \geq 0.05$ ).

Table 1.4: Comparison in mean between induction and post induction for clinical parameters in group B

Variable	Group(B) Mean $\pm$ Std. Dev	P-Value
<b>Mean Arterial Pressure (MAP)</b>		
Induction	92.4 $\pm$ 10.81	<b>0.335</b>
Post Induction	94.46 $\pm$ 10.49	
<b>Pulse Rate (beat/min) (PR)</b>		
Induction	87.62 $\pm$ 7.88	<b>0.769</b>
Post Induction	87.1 $\pm$ 9.66	

**Onset time**

The comparison between study groups by the mean time of onset is shown in table (1.5). In this study, means of time of onset were significantly higher in Group A than that in Group B (61.12 versus 44.41 sec, P= 0.001).

**Table 1.5: Comparison between study groups by mean of onset time of action**

Time of onset (sec)	Study Group		P-Value
	Group A	Group B	
	Mean ± SD	Mean ± SD	
	61.12 ± 7.11	44.41 ± 12.96	<b>0.001</b>

**Duration of action**

The comparison between study groups by mean of duration of action is shown in table (1.6). In this study, mean duration of action was higher in Group B than that in Group A but statistically not significant (40.87 versus 34.61 mints, P= 0.063).

**Table 1.6: Comparison between study groups by mean of duration of action**

Variable	Study Group		P- Value
	Group A	Group B	
	Mean ± SD	Mean ± SD	
Duration of action (mints)	34.61 ± 12.54	40.87± 13.17	<b>0.063</b>

**DISCUSSION:**

We found that a 20 ml saline flush and hand elevation immediately after a Rocuronium bolus shortened the measured onset time. Furthermore, saline flush administration prolonged the clinical duration, but it is not significant. The onset time was significantly decreased by a 20ml saline flush. Circulation components such as cardiac output, circulation time to muscle, and muscle perfusion are factors that determined the clinical effect of NMBD<sup>14</sup>. Because the normal saline flush significantly decreased the onset time, Rocuronium may be move quickly from the peripheral vein into the central vein. One mechanism demonstrating the short onset time in group with saline flush the decreased transit time from the peripheral administration site to the muscle.

Harrison and Junius<sup>18</sup> had results agree with our study. Behrendt et al.<sup>19</sup> found that giving flush of normal saline after contrast material increased the peak plasma concentration of the contrast material.

Weiss et al.<sup>20</sup> reported that giving flush normal saline increasing cardiac output lead to

a decrease in the transit time of indocyanine green. Yamaguchi et al.<sup>21</sup> reported the volume of saline flush that was enough to change the pharmaco-dynamic indices of Rocuronium, including the onset time was 18ml for antecubital and subclavian veins and 30ml for a forearm vein.

**CONCLUSION:**

In conclusion, a 20ml saline flush and hand elevation immediately after administering a Rocuronium bolus of (0.6 mg/kg) decreased the onset time and without significantly increasing the recovery phase of Rocuronium. Therefore, onset time may not decrease with a 20 ml saline flush when administering neuromuscular blockade during a hemodynamically unstable state. We recommend the use of 20ml flush and hand elevation after Rocuronium injection as a safe method to get rapid onset for intubation especially when Suxamethonium is contraindicated.

## REFERENCE:

1. Rhona CF Sinclair, BMed Sci, BM BSMRCY Mark C Luxton, BM FRCA Continuing Education in Anaesthesia & Critical Care & Pain, vol.5 issue Z April 2005 pages 45-48.
2. El-Orbany M, Connolly LA. Rapid sequence induction and intubation: current controversy. *Anesth. Analg.* 2010;110:1318-25.
3. Karamaz A, Kaya S, Turhanoglu S, Ozyilmaz MA. Effects of high-dose propofol on succinylcholine-induced fasciculation and myalgia. *Acta Anaesthesiol Scand.* 2003;47:180-4.
4. Levine M, Brown DF. Succinylcholine-induced hyperkalemia in a patient with multiple sclerosis. *J Emerg Med.* 2012;43:279-82.
5. Al-Khafaji AH, Dewhirst WE, Cornell CJ Jr, Quill TJ. Succinylcholine-induced hyperkalemia in a patient with mucositis secondary to chemotherapy. *Crit Care Med.* 2001;29:1274-6.
6. Butterworth J, Mackey D, Wasnik J. Morgan and Mikhail's Clinical Anesthesiology. 6<sup>th</sup> edition 2018 McGraw-Hill v.
7. Moore EW, Hunter JM. The new neuromuscular blocking agents: do they offer any advantages? *Br J Anaesth.* 2001;87:912-925 [[PubMed](#)]
8. Tuba Z, Maho S, Vizi ES. Synthesis and structure-activity relationships of neuromuscular blocking agents. *Curr Med Chem.* 2002;9:1507-1536. [[PubMed](#)]
9. Bevan DR. Fifty years of muscle relaxants. *Acta Anaesthesiol Scand Suppl.* 1995;106:2-6. [[PubMed](#)]
10. Yentis S, Hirsch N, Ip J. Anaesthesia and Intensive care Care A-Z: An Encyclopaedia of principles and practice, 5th ed. 2013. Churchill Livingstone.
11. Foldes FF. Fine tuning the priming principle. *Anesthesiology.* 1985;63: 560-1.
12. Koh KF, Chen FG. Rapid tracheal intubation with atracurium; the timing principle. *Canadian Journal of Anesthesia* 1994;41:688-93.
13. Han T-H, Martyn JAJ. Onset and effectiveness of rocuronium for rapid onset of paralysis in patients with major burns: priming or large bolus. *British Journal of Anaesthesia* 2009;102:55-60.
14. Donati F. Onset of action of relaxants. *Canadian Journal of Anesthesia* 1988;35:S52-8
15. Nitahara K, Sugi Y, Shigematsu K, Kusumoto G, Abe S, Higa K. Effect of bolus injection of 20ml saline with arm elevation on the onset time of vecuronium administered via a peripheral vein; a randomized controlled trial. *Anesthesia* 2013;68:904-907 [[PubMed](#)].
16. Ali HH, Utting JE, Gray TC. Quantitative assessment of residual antidepolarizing block. Part I. *Br J Anaesth* 1971; 43:473-7.
17. Ali HH, Utting JE, Gray TC. Quantitative assessment of residual antidepolarizing block. Part II. *Br J Anaesth* 1971; 43:478-85.
18. Harrison GA, Junius F. The effect of circulation time on the neuromuscular action of suxamethonium. *Anaesth Intensive Care.* 1972;1:33-40
19. Behrendt FF, Jost G, Pietsch H, Keil S, Mottaghy FM, Günther RW, Mahnken AH. Computed tomography angiography: the effect of different chaser flow rates, volumes, and fluids on contrast enhancement. *Invest Radiol.* 2011;46:271-6
20. Weiss M, Reekers M, Vuyk J, Boer F. Circulatory model of vascular and interstitial distribution kinetics of rocuronium: a population analysis in patients. *J Pharmacokinetics Pharmacodyn.* 2011;38:165-78
21. Yamaguchi I, Kidoya E, Suzuki M, Kimura H. Evaluation of required saline volume in dynamic contrast-enhanced computed tomography using saline flush technique. *Comput Med Imaging Graph.* 2009;33:23-8.