



Anesthesiology

A COMPARATIVE STUDY OF ROCURONIUM PRIMING, MAGNESIUM PRE-TREATMENT AND THEIR COMBINATION IN NEUROMUSCULAR BLOCKING CHARACTERISTICS AND QUALITY OF TRACHEAL INTUBATING CONDITIONS.

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ABSTRACT

Background and Aim : Priming principle produces a relatively rapid and profound neuromuscular blockade to ensure suitable conditions for endotracheal intubation. This study was done to compare Rocuronium priming, Magnesium pre-treatment and their combination to assess the characteristics and quality of tracheal intubating condition.

Methods : This double-blinded, randomised controlled prospective study was carried out at a tertiary health care hospital on patients undergoing surgical procedure under general anaesthesia. 60 ASA I or II patients were randomly allocated into 4 groups (n=15) as control (group R), Prime (group RP), Magnesium (group RM), Magnesium and Prime (group RPM). The hemodynamic parameter and intubating conditions were studied and statistically analysed using chi-square test and one-way ANOVA test.

Result : Magnesium sulphate pre-treatment and priming with Rocuronium provided faster onset of NM blockade (51.6 sec in group RPM when compared to 139.6 sec in group R) with excellent intubating condition.

Conclusion : Pre-treatment with both magnesium sulphate and a priming dose of Rocuronium provided faster onset of neuromuscular blockade and superior intubating conditions for rapid sequence intubation, compared with magnesium sulphate or priming alone.

KEYWORDS : Priming, endotracheal intubation, rocuronium, intubating condition

INTRODUCTION

Rapid-sequence induction and intubation clinical scenarios are situations associated with difficult tracheal intubation, because in these cases, the intensity of neuromuscular blockade at the time of laryngoscopy will be insufficient as enough time is not available for the neuromuscular blocking drugs to have their effect.

Succinylcholine once considered to be the first choice muscle relaxant in rapid sequence induction has lost its credibility on account of its serious complications and contraindications. Rocuronium was the one which showed promising results as an alternative to succinylcholine, especially when it's used in large doses.

Injection of a small dose of NDMR, known as the priming dose, before administration of the full intubating dose have shown to hasten the onset of blockade without affecting NM recovery. This Priming principle is based on the theory that a small dose of non depolarizing muscle relaxant can block large number of Acetylcholine receptors at the NM junction before appreciable clinical reduction in neuro muscular transmission occurs. The second larger dose blocks the remaining receptors and produces more rapid onset intubating conditions. After a single ED95 dose, the peak effect of Rocuronium is 4.1 minutes. Thus an intubating dose of Rocuronium should be preceded by the priming interval of at least 3 minutes. Ideal priming dose for non depolarizing muscle relaxant is 20% of ED95 or 10% of intubating dose.

Another method is the use of magnesium sulphate, which can hasten the onset of NM blockade produced by Rocuronium; the mechanism is thought to be mainly by reducing the presynaptic release of acetylcholine.

In this study, we used a combination of magnesium sulphate and a priming technique to investigate whether this could further accelerate the onset of NM blockade so that this combination can be used during rapid-sequence intubation. Secondary outcomes included duration of NM blockade and tracheal intubating conditions.

AIM OF THE STUDY

This study was done to evaluate the effect of intravenous Magnesium sulphate pre-treatment and a priming technique with Rocuronium used as a combination in the NM blockade onset, duration and quality of tracheal intubating conditions

Materials and Methods

60 ASA I and II patients undergoing elective surgical procedures under General Anaesthesia in a tertiary care hospital who satisfy the inclusion criteria were studied. History, clinical examination, blood investigations, X-ray chest and ECG were done.

INCLUSION CRITERIA :

Patients belonging to ASA Physical status I & II, age group between

18-65 years, body mass index 18.5-25.0 kg/m² and modified mallampati grade I and II were included.

EXCLUSION CRITERIA :

Patients with NM disorders, renal or hepatic failure, allergy to the study drugs, pregnancy and an anticipated difficult airway were excluded.

Written informed consent was obtained from all patients.

After connecting routine monitoring including pulse oximetry, NIBP, ECG patients were randomly allocated into four groups namely Group R (Control), Group RP (Prime), Group RM (Magnesium), Group RPM (Magnesium and Prime) using opaque sealed envelopes.

Patients in Group R received 200 ml Normal saline over 10 minutes followed by 0.6mg/kg of inj. Rocuronium intravenously; patients in the RP group received

200 ml Normal saline over 10 minutes followed by 0.06 mg/kg inj. Rocuronium 3 minutes prior to a further dose of 0.54 mg/kg of inj. Rocuronium; patients in the RM group received inj. Magnesium sulphate 50 mg/kg dissolved in 200 ml NS and infused over 10 minutes before a bolus dose of inj. Rocuronium 0.6 mg/kg; those in the RPM group was given both inj. Magnesium sulphate 50 mg/kg and inj. Rocuronium 0.06 mg/kg and after 3 minutes 0.54 mg/kg IV bolus. NM monitoring was done with a nerve stimulator using Train of Four method. Tracheal intubation was done after disappearance of response to all the stimuli except the first one. Time to onset of NM blockade was the primary outcome; Duration of NM blockade and quality of intubating conditions was also measured.

Data thus obtained is analysed using Microsoft Excel software. Statistical analysis was done using Chi-square test and oneway ANOVA, wherever applicable.

STATISTICS AND RESULTS**TABLE:1 AGE DISTRIBUTION**

Age (Years)	RP		R		RM		RPM		Total		Statistical Inference
	(n=15)	(100%)	(n=15)	(100%)	(n=15)	(100%)	(n=15)	(100%)	(n=60)	(100%)	
Below 20 Yrs.	0	0.0 %	2	13.3 %	1	6.7 %	3	20.0 %	6	10.0 %	X ² =9.608 Df=12 0.650> 0.05 Not Significant
21 to 30 Yrs.	2	13.3 %	2	13.3 %	3	20.0 %	3	20.0 %	10	16.7 %	
31 to 40 Yrs.	7	46.7 %	7	46.7 %	5	33.3 %	8	53.3 %	27	45.0 %	
41 to 50 Yrs.	2	13.3 %	1	6.7 %	3	20.0 %	1	6.7 %	7	11.7 %	
51 to 60 Yrs.	4	26.7 %	3	20.0 %	3	20.0 %	0	0%	10	16.7 %	

The above table reveals that there is no significant association between various sample (RP/R/RM/RPM) groups of age.

GRAPH : 1

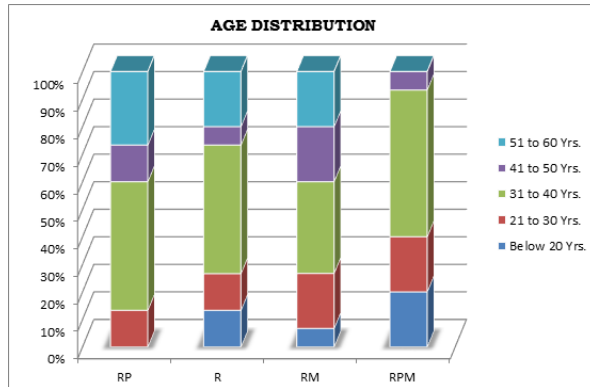


TABLE:2 Oneway ANOVA difference between various sample (RP/R/RM/RPM) groups of age

Age (Years)	Mean (Years)	S.D.	SS	Df	MS	Statistical Inference
Between Groups			833.17	3	277.706	F=2.114 0.109> 0.05 Not Significant
RP (n=15)	41.07	11.517				
R (n=15)	37.60	13.021				
RM (n=15)	39.87	12.733				
RPM (n=15)	31.40	7.818				
Within Groups			7355.867	56	131.355	

There is no statistically significant difference with respect to the distribution of age within a group and among the four groups.

TABLE:3 WEIGHT DISTRIBUTION

Weight (Kg)	Mean (Kg)	S.D.	SS	Df	MS	Statistical Inference
Between Groups			325.667	3	108.556	F=1.501 0.224> 0.05 Not Significant
RP (n=15)	53.27	10.457				
R (n=15)	49.33	6.218				
RM (n=15)	51.07	7.620				
RPM (n=15)	55.53	9.117				
Within Groups			4048.933	56	72.302	

p value 0.224>0.05. So the groups are comparable in terms of weight distribution.

GRAPH : 2

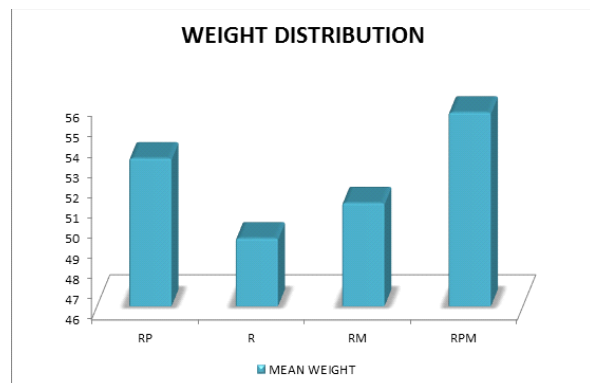


TABLE :4 HEIGHT DISTRIBUTION

Height (Centimeters)	Mean (Cms)	S.D.	SS	Df	MS	Statistical Inference
Between Groups			97.133	3	32.378	F=0.681 0.567> 0.05 Not Significant
RP (n=15)	158.67	5.690				
R (n=15)	155.93	7.535				
RM (n=15)	156.00	6.358				
RPM (n=15)	158.33	7.780				
Within Groups			2661.600	56	47.529	

p value 0.567>0.05. So the groups are comparable in terms of height distribution.

GRAPH : 3

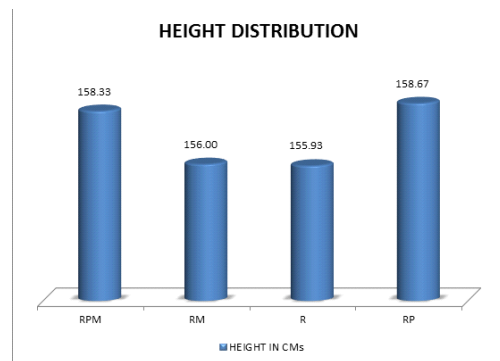


TABLE :5 BASELINE MEAN ARTERIAL PRESSURE (MAP)

MAP Base (mmHg)	Mean (mmHg)	S.D.	SS	Df	MS	Statistical Inference
Between Groups			171.108	3	57.036	F=0.839 0.478> 0.05 Not Significant
RP (n=15)	90.0067	5.45795				
R (n=15)	88.0800	5.55289				
RM (n=15)	88.9620	8.06292				
RPM (n=15)	92.5840	12.09489				
Within Groups			3806.892	56	67.980	

p value 0.478>0.05. So the groups are comparable in terms of Baseline MAP.

GRAPH : 4

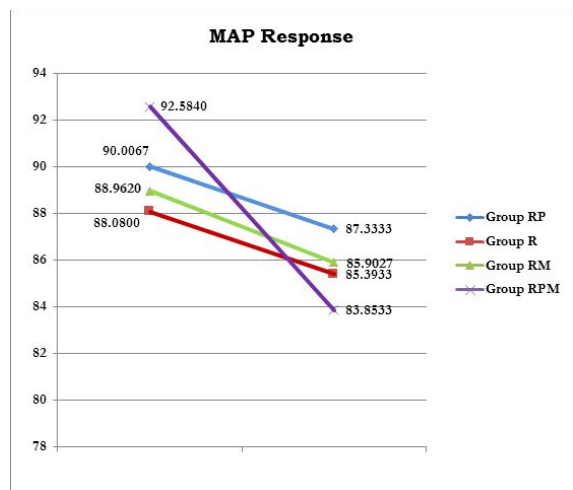
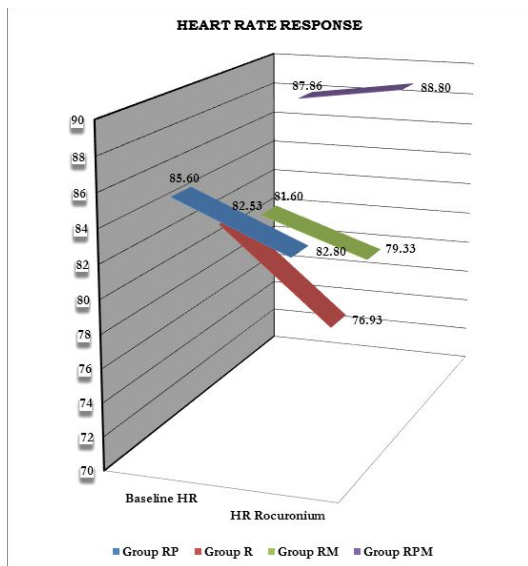


TABLE :6 BASELINE HEART RATE

HR Base (rate/min)	Mean (rate/min)	S.D.	SS	Df	MS	Statistical Inference
Between Groups			1531.400	3	510.467	F=1.426 0.223>0.05 Not Significant
RP (n=15)	85.6000	5.40899				
R (n=15)	82.5333	9.60555				
RM (n=15)	81.6000	8.04274				
RPM (n=15)	87.86	8.48528				
Within Groups			8344.533	56	149.010	

p value 0.223>0.05. So the groups are comparable in terms of Baseline HR.

GRAPH : 5**TABLE :7 MAP AT THE TIME OF INJECTION OF ROCURONIUM (MAProc)**

MAP roc (mmHg)	Mean (mmHg)	S.D.	SS	Df	MS	Statistical Inference
Between Groups			92.818	3	30.939	F=0.717 0.546>0.05 Not Significant
RP (n=15)	87.3333	4.07530				
R (n=15)	85.3933	4.66881				
RM (n=15)	85.9027	8.53012				
RPM (n=15)	83.8533	7.83371				
Within Groups			2415.501	56	43.134	

p value 0.546>0.05. So MAP at the time of injection of Rocuronium is comparable among the groups.

TABLE: 8 HR AT THE TIME OF INJECTION OF ROCURONIUM (HR roc)

HR roc (rate/min)	Mean (rate/min)	S.D.	SS	Df	MS	Statistical Inference
Between Groups			2194.86	3	731.62	F=2.363 0.125 > 0.05 Not Significant
RP (n=15)	82.8000	7.24273				
R (n=15)	76.9333	5.99365				

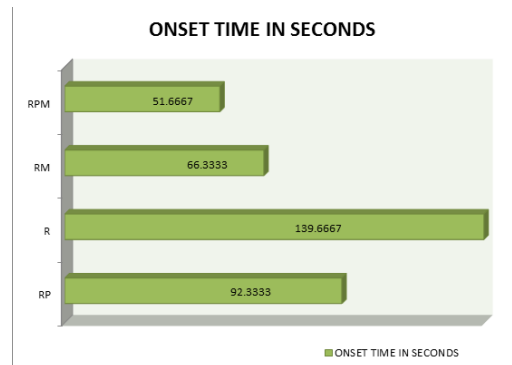
RM (n=15)	79.3333	7.76132				
RPM (n=15)	88.8000	11.31370				
Within Groups			6439.06	56	114.98	

p value 0.125>0.05. So the groups are comparable in terms of HR at the time of injection of Rocuronium.

TABLE:9ONSET OF NEUROMUSCULAR BLOCKADE

ONSET	Mean (Seconds)	S.D.	SS	Df	MS	Statistical Inference
Between Groups			67151.667	3	22383.889	F=319.498 0.000<0.05 Significant
RP (n=15)	92.3333	4.95215				
R (n=15)	139.6667	7.43223				
RM (n=15)	66.3333	13.29160				
RPM (n=15)	51.6667	4.87950				
Within Groups			3923.333	56	70.060	

There is a statistically significant difference in onset time for NM blockade among the groups as delineated by one way-ANOVA.

GRAPH :6**TABLE:10 DURATION OF NM BLOCKADE**

DURATION	Mean (Minutes)	S.D.	SS	Df	MS	Statistical Inference
Between Groups			1280.183	3	426.728	F=6.489 0.001<0.05 Significant
RP (n=15)	40.3333	2.96808				
R (n=15)	40.0000	3.27327				
RM (n=15)	44.4000	12.75483				
RPM (n=15)	51.4667	8.99100				
Within Groups			3682.667	56	65.762	

There is a statistically significant difference in duration of NM blockade among the groups as delineated by one way-ANOVA.

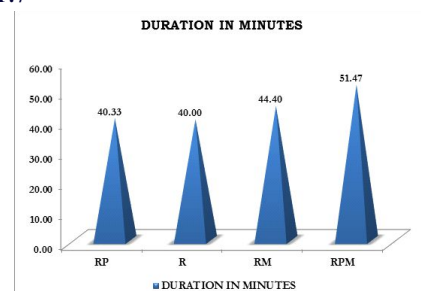
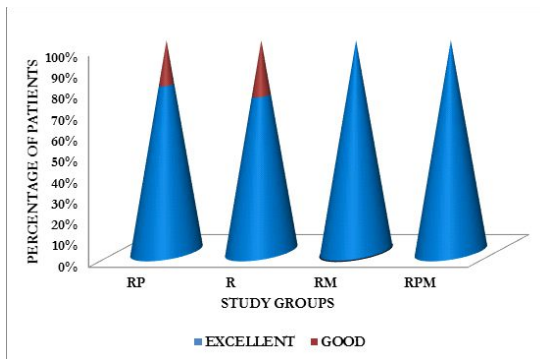
GRAPH :7

TABLE : 11 INTUBATING CONDITIONS

INTUBATING CONDITIONS	Mean	S.D.	SS	Df	MS	Statistical Inference
Between Groups			2.933	3	0.978	F=8.213 0.000<0.05 Significant
RP (n=15)	1.73	0.458				
R (n=15)	1.47	0.516				
RM (n=15)	2.00	0.000				
RPM (n=15)	2.00	0.000				
Within Groups			6.667	56	0.119	

GRAPH : 8

There is a statistically significant difference in quality of intubating conditions among the groups as delineated by one way ANOVA. Here EXCELLENT intubating conditions were given a score of two, while GOOD ones were given a score of one.

In conclusion all the four groups were comparable in terms of demographic and hemodynamic parameters. Onset of NM blockade was shortest, NM blockade duration was longest, and quality of tracheal intubating conditions was most superior in RPM Group; and these three observations were statistically significant.

DISCUSSION

In patients with a higher risk of aspiration, rapid sequence induction and intubation has been used to facilitate rapid tracheal intubation. The resultant effect by this method is to minimize time interval between loss of protective airway reflexes and tracheal intubation by using a cuffed endotracheal tube.

Succinylcholine, once considered to be the first choice muscle relaxant in rapid sequence induction has lost its credibility on account of its serious complications and contraindications. Rocuronium showed promising results as an alternative to succinylcholine, when it's used in large doses. But larger doses do not always yield rapid onset, at the same time it prolonged the duration of action.

For the controlled use of non-depolarising NMBD for RSI, the priming and timing techniques were initiated which allows a minimal induction-to-intubation interval without increasing the duration of blockade. The priming technique was introduced by Mehtha et al and shwarz et al separately in the year 1985. The first group used Pancuronium while the second used Vecuronium. Ortiz-gomez et al stated the differences in tracheal intubating conditions one minute after administering succinylcholine 1mg/kg, and 0.6mg/kg Rocuronium with no priming, 0.57mg/kg Rocuronium four minutes after using different priming techniques. A significant change in onset between all comparisons were found.

Other methods to reduce the onset time of NM blockade was experimented. The study on the basis of priming technique before the onset and tracheal intubating conditions in burns patients and control was done by Han and Martyn. The study showed that a dose of 1.5 mg/kg Rocuronium, produced similar onset time with superior intubating conditions, when compared with usage of priming techniques.

Another modality by which we can hasten the NM blockade onset of Rocuronium is by using Magnesium sulphate. The mechanism of action is by reducing the presynaptic release of acetyl choline.

In this study, magnesium sulphate was combined with a priming

technique and the acceleration of NM blockade onset time occurred was investigated. Onset, duration of NM blockade and quality of intubation conditions were also looked for.

When compared among the four groups for duration of blockade, onset time was shortest for magnesium and prime group ($p<0.001$) which was statistically significant.

The onset of NM blockade was reduced when compared to control by 34%, 52% and 73% with priming, magnesium sulphate and combination of magnesium sulphate and priming respectively, which is comparable with previous studies (19% and 36% with priming and magnesium sulphate respectively) done by Naguib et al.

A study done by Magorian et al with suxamethonium (1mg/kg) and higher dose of rocuronium (12mg/kg) had 40% and 39% faster onset times respectively, when compared with a standard dose of Rocuronium (0.6mg/kg). Hence it is concludable that magnesium and priming combination method can ensure faster NM blockade than that obtained with suxamethonium.

While comparing magnesium and prime group with that of magnesium group the results showed a significant smaller SD and variance. Therefore the magnesium sulphate/ priming combination facilitates initiation of NM blockade, decreased variability of onset time and also provides a more predictable onset while comparing with magnesium sulphate group.

It was observed in our study that the duration of NM blockade increased by 9% and 22.33% in the RM and RPM group respectively. In an earlier study conducted by Czarnetzki et al showed that the duration of NM blockade was increased by magnesium sulphate by 27-34%, but the amount of rocuronium required to maintain adequate NM blockade during surgery is reduced by magnesium sulphate.

The onset period was 136.6 sec with rocuronium 0.6 mg/kg when compared with 90 sec in an earlier experiment conducted by Naguib M et al. Factors that influence the onset time are : BMI, anesthetic agents, modes or devices of nerve stimulation and definition of onset time.

There was no serious complications observed with magnesium sulphate (50-60 mg/kg). Priming with 0.06 mg/kg rocuronium did not cause any complication such as low PaO₂, respiratory difficulty/ aspiration as observed by MH Kim, A.Y.Oh, Y.T.Jeon, J.W Hwang and S.H do et al, who did a similar study in 2012; they had set a uniform time interval of 40 secs in between bolus dose of Inj. Rocuronium and intubation. But in our study we intubated the patients after all the stimuli was absent, except for the first one in TOF monitoring; there by we could make proper assessment of intubating condition and onset of NM blockade.

To conclude, a rapid onset of NM blockade and superior intubating conditions is made possible by pretreatment with both magnesium sulphate and a priming dose of Rocuronium than with magnesium sulphate or priming alone.

CONCLUSION

A rapid onset of NM blockade (51.6 seconds in group RPM when compared to 139.6 seconds in group R) and superior tracheal intubation conditions is made possible by pretreatment with both magnesium sulphate and a priming dose of Rocuronium than with magnesium sulphate or priming alone. So this technique can be safely employed for Rapid Sequence Induction and Intubation.

REFERENCES:

- [1] M.H. Kim, A.Y. Oh, Y.T. Jeon, J.W. Hwang and S.H. Do, (2012). A randomized controlled trial comparing rocuronium priming, magnesium pre-treatment and a combination of the two methods. *Anaesthesia*, 67, 748-754.
- [2] El-Orbany M, Connolly LA, (2010). Rapid sequence induction and intubation : Current controversy. *Anesthesia and Analgesia*, 110, 1318-25.
- [3] Schmidt J, Irouschek A, Muenster T, Hemmerling tM, Albrecht S, (2005). A priming technique accelerates onset of neuromuscular blockade at the laryngeal adductor muscles. *Canadian Journal of Anaesthesia*, 52, 50-4.
- [4] Griffith KE, Joshi GP, Whitman PF, Garg SA, (1997). Priming with rocuronium accelerates the onset of neuromuscular blockade. *Journal of Clinical Anaesthesia*, 9, 204-7.
- [5] Bock M, Haselmann L, Bottiger BW, Motsch J, (2007). Priming with Rocuronium accelerates neuromuscular block in children : a prospective randomized study. *Canadian Journal of Anaesthesia*, 54, 538-43.
- [6] Leykin Y, Pellis T, Lucca M, Gullo A, (2005). Effects of ephedrine on intubating conditions following priming with rocuronium. *Acta Anaesthesiologica Scandinavica*, 49, 792-7.

- [7] Czarnetzki C, Lysakowski C, Eila N, Tramer N, (2010). Time Course of rocuronium induced neuromuscular block after pre-treatment with magnesium sulphate: a randomized study. *Acta Anaesthesiologica Scandinavica*, 54, 299-306.
- [8] Magorian T, Flannery KB, Miller RD, (1993). Comparison of Rocuronium, Succinylcholine and vecuronium for rapid-sequence induction of anaesthesia in adult patients. *Anesthesiology*, 79, 913-18.
- [9] Siber TJ, Zibenden AM, Curatolo M, Shorten GD, (1998). Tracheal intubation with Rocuronium using the timing principle. *Anaesthesia Analgesia*, 86, 1137-1140.
- [10] Kofman AF, Khan AN et al, (2001). Pre-curarization and Priming : A theoretical analysis of safety and timing. *Anaesthesia analgesia*, 93, 1253-1256.
- [11] Feldman SA, (1994). Rocuronium, Onset time and intubating condition. *European Journal of Anaesthesia suppl*. 9, 49-52.
- [12] Leykin Y, (2005). Intubating conditions following Rocuronium : influence of induction agent and priming, *Anaesthesia intensive care*, 33, 462-468.
- [13] Naguib M, (1994). Different priming techniques, including mivacurium, accelerate the onset of rocuronium. *Canadian Journal of Anaesthesia*, 41, 902-7.
- [14] Topcuoglu PT, Uzun S, Canbay O, Pamuk G, Ozgen S, (2010). Ketamine, but not priming, improves intubating conditions during a propofol-rocuronium induction. *Canadian Journal of Anaesthesia*, 57, 113-9.
- [15] Lee HJ, Kim KS, Yeon JT, Suh JK, Sung IH, Shin IC, (2010). Potency and recovery characteristics of rocuronium mixed with sodium bicarbonate. *Anaesthesia*, 65, 899-903.
- [16] Lee H, Kim K, Jeong J, Cheong M, Shim J, (2009). Comparison of the adductor pollicis, orbicularis oculi, and corrugators supercilii as indicators of adequacy of muscle relaxation for tracheal intubation. *British Journal of Anaesthesia*, 102, 869-74.