Effect of priming technique and single intubating dose technique on rapid sequence intubation with rocuronium using train of four monitoring

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Abstract

Aim: Rocuronium bromide has fastest onset time among non- depolarizing muscle relaxants; hence a safe alternative for RSI when the priming principle is used. The primary aim of this study was to compare the intubating conditions with priming technique and single intubating dose technique with rocuronium and to assess the onset time of rocuronium using Train of Four (TOF) monitoring.

Materials and Methods: We conducted a randomized, prospective study in 60 patients of ASA I and II in age group of 20-50 years posted for surgeries under general anesthesia and divided into two groups of 30 each. In Group I priming was done with 1 ml of normal saline and Intubating dose of rocuronium 0.6mg/kg was given. In group II priming was done with 1/10th i.e 0.06 mg/kg (1ml) of the total intubating dose followed by remaining dose of 0.54 mg/kg. In both the groups intubating doses of rocuronium were diluted to 10 ml of normal saline. TOF stimuli was used to assess the time of onset of intubation and Cooper scoring system was used to compare the intubating conditions.

Results: Patients intubated in the priming group showed a faster onset time (61. 97 sec) than single intubating dose group (114.57) with successful intubation in both the groups. Excellent intubating conditions were seen in 97% patients and good intubating conditions in 3% patients of both the groups.

Conclusion: Both priming technique and single intubating dose technique produces excellent intubating condition in majority (97%) of the patients with priming technique showing rapid onset time compared to single intubating dose technique.

Keywords: Rocuronium, Priming, Time of intubation, Intubating condition.

Introduction

Rapid sequence intubation (RSI) technique is of utmost significance in patients vulnerable to aspiration such as full stomach, intestinal obstruction and general anaesthesia for emergency or elective caesarean section. The risks involved in RSI are failure to ventilate, heart rate changes, blood pressure variations and airway trauma. To avoid such undesirable side effects a modification of standard RSI technique has come up that includes preoxygenation, induction, cricoid pressure and gentle positive pressure ventilation. Modified RSI allows anaesthetist to confirm the ability to ventilate and to decide for awake intubation if ventilation failure occurs.

Succinylcholine (Sch), a depolarising muscle relaxant was the drug of choice for RSI.[1] It produces profound muscle relaxation but has many undesirable side effects[2-4] that are related to the depolarising action of Sch. Hence nondepolarising muscle relaxants (NDMR) and newer techniques have evolved for rapid and smooth induction. But onset of action of NDMR is slow. So different approaches like increasing the single intubating dose of NDMR, combination of relaxants, priming dose, increased concentration of inhalational and intravenous agents are in use to potentiate neuromuscular blockade.[4] One such technique is timing technique where a single bolus dose of muscle relaxant is administered and the period from induction to complete muscle relaxation is noted. Rocuronium bromide has the fastest onse time among non depolarisers. When used with priming technique, it can be considered as an alternative to succinylcholine. In priming technique, a small dose (1/10th) of non depolarising drug which should not cause any unpleasant side-effects is used.[5] After 2-4 minutes of this small dose, a greater intubating dose produces suitable condition for endotracheal intubation.[6] While using either priming dose or single intubating dose technique for accuracy, precision and minimal instability, Train of four monitoring (TOF) is helpful in rapid sequence intubation (RSI) in anaesthetised patients. It was first described by Ali et al in 1970.[7] Onset of neuromuscular block is assessed by TOF stimulus with loss of visual response of adductor pollicis muscle by stimulating ulnar nerve which is the best site for monitoring. In this study, we evaluated the technique most suitable to achieve optimum conditions for rapid sequence intubation using train of four monitoring and rocuronium as muscle relaxant. 60 patients of ASA I or II in age group of 18-60 years, scheduled for surgeries under general anaesthesia were taken and divided randomly into 2 groups of 30 each. In Group I i.e timing or single bolus intubation technique, priming was done with 1 ml of normal saline followed 3 mins later by IV rocuronium 0.6mg/kg bolus. In Group II, Priming was done with IV rocuronium 0.06mg/kg followed 3 minutes later by rest of the total dose 0.54mg/kg.

Materials and Methods

Our study was conducted in anaesthesia department of Maharishi Markandeshwar Institute of Medical Sciences and Research Hospital after approval of institution Ethical committee. Patients selected for the study were briefed about the method and nerve stimulation technique; written

informed consent was taken. Investigations were carried out one day before the surgery. On the operative day, in operating room wide bore intravenous cannula was secured and lactated ringer initiated. Baseline monitoring like ECG, NIBP, SpO2 and $EtCO_2$ was done. We noted the baseline parameters. Peripheral nerve stimulator was used to set a supramaximal stimulus. 10mins before giving the priming dose, patients in both the groups were given Inj butorphanol 30 mcg/kg IV, inj midazolam 0.03 mg/kg IV and Inj glycopyrrolate 0.2 mg IV 10 min prior to the priming dose.

In Group I priming was done with 1 ml of normal saline and Intubating dose of rocuronium 0.6mg/kg was given. In group II priming was done with $1/10^{th}$ i.e 0.06 mg/kg (1ml) of the total intubating dose followed by remaining dose of 0.54 mg/kg. In both the groups intubating doses of rocuronium were diluted to 10 ml of normal saline.

After priming, patients were enquired for having any complaints of ptosis, diplopia, dysphagia, dyspea, myalgia by the investigator who was blinded to the study. Three minutes after giving the priming dose, inj Etomidate 0.3 mg/kg I/V and intubating dose of rocuronium was given for induction following which we performed modified rapid sequence intubation.

On the ulnar nerve at the wrist, a supramaximally set TOF stimuli was applied after giving the intubating dose of rocuronium. Testing at 10 mA above the lowest current at which four responses can be elicited provided values that are consistent with those of supramaximal testing. We repeated TOF every 10 sec and noted till the disappearance of T_1 of TOF. "Onset time of intubation." was the time lag in giving the intubating dose and the disappearance of T_1 of TOF.

After T_1 was lost, endotracheal intubation with modified RSI technique was done and intubation score was recorded. Intubating conditions were graded as excellent if intubating scores were between 8- 9, good with 6–7, fair with 3–5 and poor with 0-2.

Cooper et al scoring system

Score	Jaw relaxation	Vocal cord	Response to stimulation
0	Poor (impossible)	Closed	Severe cough or bucking
1	Nominal (difficult)	Closing	Mild cough
2	Moderate (fair)	Moving	Slight diaphragmatic Movement
3	Good (easy)	Open	None

Monitoring was done with SpO_2, ECG, NIBP and $EtCO_2$. Onset time of intubation, intubating score and intubating conditions at the time of intubation was noted. Anaesthesia was maintained by O_2, N_2O (50:50), inhalational anaesthetics and NDMR. Patients were reversed after culmination of surgery with Inj neostigmine 0.05mg/kg IV and Inj glycopyrrolate 0.01mg/kg IV. Later on patients were shifted to recovery room for further monitoring.

Statistical Analysis

The data was entered in excel sheet and then analysed using SPSS (Statistical Package for the Social Science) 21 version. Statistical analysis was done for all quantitative variables in each group. Range, standard deviation (± SD), median, frequencies and percentages were compared between the groups. Student t – test and Maan- Whitney U test was used for independent samples for parametric and non-parametric data. Repeated ANOVA test was used for calculating difference between time periods. Chi square test ($\chi 2$) was performed for comparing categorical data. P-value of less than 0.05 was considered statistically significant.

Observations and Results

Table 1: Distribution of patient according to age and weight

	Group I		Group II		T	P-Value
	Mean	SD	Mean	SD		
Age (in Years)	31.47	12.06	36.33	11.16	-1.622	0.110
Weight (in KG)	61.03	10.91	58.13	14.00	0.895	0.375

Table 2: Intubating conditions

		Group		Total
		I	II	
Intubating Conditions	Excellent	29	29	58
	Good	1	1	2
Total		30	30	60

Table 3: Onset time and intubating score

	Group I		Group II		T	P-value
	Mean	SD	Mean	SD		
Onset Time (In Seconds)	114.57	15.66	61.97	7.84	-6.565	0.000
Intubating Score	8.67	0.55	8.77	0.50	-0.853	0.394

Results

The patients were demographically similar in both groups (Table 1). Both groups had excellent intubating condition in 29 patients (97%) while 1 patient (3%) had good intubating condition and none of the patient showed fair and poor intubating conditions in either of the group (Table 2). The mean onset time recorded in single intubating technique i.e. Group I was 114.57 while in Group II i.e. in priming technique 61.97 seconds was the onset time. There was a highly significant difference between the two groups with a p value of 0.000 (Table 3). Mean Intubating score in Groups I and II were 8.67 and 8.77 respectively, which was comparable with non significant p value.

Discussion

General anaesthesia leads to blunting of the protective reflexes in anaesthetized patients and makes them susceptible to gastric regurgitation. Rapid sequence induction (RSI) and intubation is required to prevent aspiration and emergency protection of airway in patients with haemodynamic imbalalance, difficult gas exchange and surgical emergencies.[8] We opted for modified RSI because it permits positive pressure ventilation and decreases the chance of fall in SpO_2 hence avoiding hypoxia.[9]

The induction-intubation time needs to be minimized; hence an agent which has fast onset of action and is short acting is required for RSI. Succinylcholine (Sch) has been the gold standard muscle relaxant used in RSI as it has an onset of 40-60 seconds and duration of 6-10min. But it has undesirable problems associated with it[10] like myalgia due to muscular fasciculations, hyperkalaemia, masseter spasm, bradycardia, increase in potassium levels increasing the risk of cardiac arrest, malignant hyperthermia with increased intracranial, intra-ocular, and intragastric and intracranial pressures[11] There is contraindication to use Sch in neuromuscular diseases, crush injuries and in burns.[12] These negative effects succinylcholine have prompted to search for its alternatives and increased use of NDMR.

Non depolarising agents like pancuronium, vecuronium and atracuronium do not achieve acceptable intubating conditions as rapidly as Sch.[12] Rocuronium is the fastest acting NDMR which is believed to be primarily due to its low potency.[13,14]

Rocuronium is the only certified NDMR which can be used instead of Sch for intubation due to its fast onset of action[15] (60-90 sec) and intubating conditions that are similar to that of Sch[12] but it has a longer duration of action. The only condition where it is contraindicated is hyper-sensitivity reaction. But it should be carefully used in patients of myasthenia gravis, liver disease and severely cachexic patients, as the time of action of rocuronium may be drastically prolonged.[16]

Studies of RSI intubations using etomidate with rocuronium or succinylcholine showed comparable results at first intubation attempts.[17]

Rocuronium has become a popular substitute of sch for RSI in view of the side effects of sch, especially with the introduction of suggamadex.[18,19] It has a rapid onset time, good cardiovascular stability and causes no histamine release.[20] Dose of Rocuronium of 0.6-1.2 mg/kg is comparable to Sch 1 mg/kg in providing acceptable intubation conditions.[15] Increasing the doses will produce neuromuscular block lasting for a longer time. Sudha P et al observed a duration of action of 37.9 ±6.1 minutes with 0.6mg/kg rocuronium i.e duration of action is increased by 3.75 times that of Sch.[27] Chavan et al found that 0.9mg/kg rocuronium has an action for 49.3+ 8.7 min i.e. prolongs it by 7.5 times that of Sch.[15] This is undesirable in case of short and medium duration surgeries. We took 0.6 mg/kg as intubating dose of rocuronium as was taken by Chathrath Veena et al who postulated that intubating conditions were similar with Sch 2mg/kg and rocuronium 0.6mg/kg at 60 s.[23]

Different methods are in use to decrease reduce the onset time of intubation along and to provide satisfactory intubating conditions that are helpful in rapid sequence intubation. These methods include combining the muscle relaxants, timing principle, priming principle and large dose NDMR. Larger doses of rocuronium as used in timing technique delay recovery and needs proper adjustment of induction times to avoid side effects. Priming principle is one of the techniques where a little dose (10% of intubating dose) of NDMR is given followed by a greater dose for intubation after 2-4 min. This fastens the onset of neuromuscular block along with adequate intubating conditions for endotracheal intubation without undue prolongation of action or undesirable side effects. This technique is preferable in all patients who required rapid sequence intubation and in whom succinylcholine is undesirable.[6]

In our study, rocuronium has been used with intubation dose of 0.6 mg/kg (i.e. 2xED95) and priming dose of 0.06 mg/kg at a priming interval of 3 min. Yavascaoglu et al observed quicker onset time and better intubating conditions with priming interval of 3 min as compared with 2 min interval.[21] Sridhar et al also got better results with 3 minutes priming interval than 2 minutes.[22]

Kwon et al observed that the modified rapid sequence intubation (RSI) with rocuronium had similar intubation conditions and similar complications as those of conventional RSI with Sch.[24]

It is postulated that a little dose of NDMR blocks many acetylcholine receptors at the neuromuscular junctions (NMJ) before clinical reduction in neuromuscular transmission. The second greater dose blocks the rest of the receptors leading to faster drug onset. While the priming principle is applied to fasten Neuromuscular block is hastened by priming principle where the prior small dose is 10% of the intubating dose. The priming method is better than the bolus/timing method in all planned cases and in cases where Sch is CI.[6]

Studies by Griffith et al & Rao et al established that priming principle applied to Rocuronium decreased the onset time by 42% and 46% respectively.[4,26]

Most of the studies prove that onset of action of Rocuronium is decreased using the priming principle but the amount of reduction in onset time of action is different as

per different studies.[4,26] It was found to be at 34 +/- 6 seconds by Griffith et al and 50.67 +/- 7.39 seconds by Rao et al in the priming group. Contrary to our study, Md. Liaquatunnoor et al did not find any statistically significant difference between the priming and timing technique of intubation (p=0.329).This may be due to the difference in the anaesthesia protocols as they used Inj. Thiopentone sodium 5.0 mg/kg as induction agent.[28] Intubating conditions are dependent on the depth of anaesthesia apart from neuromuscular blockade.

Jose A et al.[29] found faster onset with priming interval of 4 min while Yavascaoglu B et al.[21] found satisfactory RSI with rocuronium with 3 minutes priming interval. The differences in priming interval also add to the variations observed in the onset of time of action.

In our study, we assessed intubating conditions with Cooper et al scoring. None of the patient had poor or minimal jaw relaxation in either group. Intubating scores were 8.67 in group I and 8.77 in group II.

The intubation score was observed when T_1 response of TOF was lost. The onset time of intubation was 61.97± 7.84 sec in group II compared with 114. 57 ± 15.66 in group I. Our results were concurrent with the study done by Jeevarathnam[31] et al, Griffith[26] et al and Md. Liaquatunnoor[28] et al who also found no significant difference between the groups in jaw relaxation, vocal cord movement and response to intubation.

In both the group, we got excellent intubating conditions in 97% of patients and good intubating conditions with 3% patients. Our result was similar to that of Rao et al.[4] Our result was also concurrent with the study of Soo Kyung Lee et al[30] who observed good-to-excellent intubating conditions in patients getting priming dose of 0.06mg/kg of rocuronium bromide follow by administration of the intubating dose of rocuronium bromide 0.54 mg/kg and in those administered receiving single dose 0.60 mg/kg of rocuronium bromide.

Our study is also consistent to DS Shashank[6] et al who compared intubation conditions with pretreatment of rocuronium, vecuronium and atracuronium ion and observed good to excellent intubating conditions within 60 secondswith pretreatment of rocuronium.

M Hanumantha Rao[4] also found that priming with rocuronium produces excellent intubating conditions with onset in 60 sec.

In our study no patient had evidence of side effects of priming like weakness, diplopia, dysphagia and dyspnea. The reason for this may be that we used very little priming dose of 0.06 mg /kg. Hanumantha et al also got no side effect while using a priming dose of 0.06 mg/kg.[4]

Conclusion

From the study done and data analysed, we conclude that both timing and priming techniques can be used for RSI. Both priming technique and single intubating dose technique provide excellent intubating condition in majority (97%) of the patients. With priming technique rapid onset time can be achieved as compared to single intubating dose technique.

Conflict of Interest: None.

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