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Comparison of Efficacy of Rocuronium with Priming and Without Priming on Endotracheal Intubation in Adults.

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ABSTRACT

Rocuronium produces faster neuromuscular blockade compared with other drugs. It produces similar intubating conditions to that of succinylcholine, but it does not have short intubation time. Hence, it cannot be used for rapid sequence intubation, but rocuronium with priming may produce similar intubating time and conditions to that of succinylcholine. Rocuronium with priming can be an alternative to succinylcholine in rapid sequence intubation in conditions where latter is contraindicated. To compare the efficacy of Rocuronium with priming and without priming on endotracheal intubation in adults. 80 patients of ASA physical status I and II, aged between 18 and 60 years, of both sexes, were divided into priming and control groups of 40 each. Patients in the priming group received 0.07mg/kg of rocuronium and those in the control group received normal saline. All patients received Midazolam 0.02mg/kg and Fentanyl 2 µg/kg followed by Propofol 2 mg/kg for induction. Intubating dose of rocuronium 0.63mg/kg in the priming group and 0.7mg/kg in the control group were administered 3 min after priming. Onset time of intubation was assessed using Train of Four stimuli, and the intubating conditions were compared by the Cooper scoring system. The onset time of intubation was 38.7 ± 8.80 sec in the priming group and 60 ± 10.17 sec in the control group, with excellent intubating conditions in both the groups and without any adverse effects. Priming with rocuronium provides excellent intubating conditions in less than 60 sec with no adverse effects.

Keywords: Endotracheal intubation, intubating conditions, priming, rocuronium

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INTRODUCTION

The standard anaesthetic technique used for patients who are considered to be at risk of aspiration is known as Rapid Sequence Induction (RSI). In order to prevent aspiration, the time interval between the induction of anaesthesia and tracheal intubation should be kept as short as possible. Neuromuscular blocking agents are given as the part of RSI to facilitate a safe and rapid tracheal intubation. Clinical conditions in which producing sufficient neuromuscular blockade for intubation of trachea might be difficult includes rapid sequence intubation and resistance to several neuromuscular blocking agents. In such cases as not adequate time has been allowed for the drugs to take its effect, the depth of neuromuscular blockade at the time of intubation of trachea can be insufficient. This insufficient neuromuscular blockade might result in vocal cords not opening fully, failed intubation of trachea or poor conditions for intubation which might lead to trauma to laryngeal structures, vocal cord injury and hoarseness of voice in the postoperative period.

Succinylcholine is considered to be the drug of choice for Rapid sequence induction. But, it has a number of adverse effects like muscle fasciculation, myalgia, hyperkalemia [1], bradyarrhythmia [2], increased intra ocular tension, increased intra cranial tension [3], increased intra gastric pressure, anaphylaxis, malignant hyperthermia and masseter spasm. Hence, it is contraindicated in conditions like neuromuscular disorders, burns, acute head injury, intracranial bleed [4], open eye injury, spinal cord injury [5], cerebrovascular accidents and renal diseases. The above side effects and contraindications of succinylcholine had prompted the use of non-depolarizing muscle relaxants using various techniques for rapid sequence intubation such as timing principles [6], combination of relaxants [7, 8], high dose of non-depolarizing muscle relaxants [9], inhalational agents to augment the effect of non-depolarizing muscle relaxants [10], use of intravenous anaesthetic agents with non-depolarizing muscle relaxants to augment neuromuscular blockade [11] and priming principle.

In our study, we have used Priming principle. It is a divided dose technique of neuromuscular blocking drug, capable of producing a rapid onset of neuromuscular block and suitable intubating condition. It allows to shorten the onset time of a non-depolarizing neuromuscular blocking agent without increasing the duration of action by application of small dose few minutes prior to large intubating dose. A small priming dose (10% of intubating dose) is administered to an awake patient. After 2-4 min, the rest of the intubating dose is administered to produce neuromuscular blockade for rapid sequence intubation.

Rocuronium bromide is a non-depolarizing muscle relaxant. It has rapid onset of neuromuscular blockade and intermediate duration of action.

MATERIALS AND METHODS

After the approval of institutional ethics committee, preliminary studies were carried out in 80 consenting patients of ASA I and II aged between 18 and 60 years, of both sexes. It is a prospective randomized doubleblind placebocontrolled study conducted between June 2014 and May 2015. Patients with neuromuscular diseases, anticipated difficult intubation (obesity, Thyromental distance less than 6 cm and Mallampati grade 3 and 4), pregnancy, hepatic, renal diseases, patients receiving drugs interfering with neuromuscular action and history of allergic reaction to rocuronium were excluded from the study

Selected patients were randomly divided into two equal groups using Block randomizations:

Group A: Patients received Normal saline as priming dose + 0.7 mg/kg of Rocuronium as intubating dose and
Group B: Patients received 0.07 mg/kg of Rocuronium as priming dose + 0.63 mg/kg of Rocuronium as intubating dose

After shifting the patients to Operating Room, Electrocardiogram, non-invasive blood pressure and pulse oximetry monitors were connected. Intravenous cannula was secured and Ringer Lactate was started. Midazolam 0.02mg/kg and Fentanyl 2ug/kg body weight were given intravenously to all patients in both groups 10 min prior to priming dose. Blood pressure cuff was applied to the contralateral upper limb. The supramaximal stimulus was set with a peripheral nerve stimulator. Total intubating dose of Rocuronium bromide 0.7 mg/kg was diluted to 5 ml. For group “A”, 2 ml of Normal saline was taken in a 2 ml syringe. For group “B”, 0.5 ml Rocuronium bromide is taken from the 5 ml syringe (containing total dose) and diluted to 2

ml with Normal saline and the remaining 4.5 ml is diluted to 5ml with Normal saline. Drugs were loaded, labeled and administered by anaesthesiologist.

After pre-oxygenation with 100% oxygen, the priming dose of Rocuronium bromide 0.07 mg/kg (10% of intubating dose) or Normal saline was given 3 min before the intubating dose as per randomization. The patients were enquired about ptosis, double vision, difficulty in swallowing and difficulty in breathing. Two and half minutes after giving the priming dose, patients were induced with intravenous Propofol 2 mg/kg body weight over 20s. The intubating dose of Rocuronium was injected 3 min after the priming or normal saline injection. After giving the intubating dose of Rocuronium, a supramaximally set Train of Four (TOF) stimuli was applied over the ulnar nerve at the wrist through surface electrodes and was repeated every 12sec and assessed virtually for loss of adduction of thumb and disappearance of T1 of TOF stimuli. Time interval between the intubating dose and the loss of T1 of TOF stimuli was considered as "onset time of intubation"
After loss of T1 of TOF stimuli, the trachea was intubated by an anaesthesiologist having at least 2 years of experience and intubating conditions were noted and intubation score recorded using an intubation scoring system. Intubation conditions were graded as excellent when intubating scores are between 8 and 9, good with 6-7, fair with 3-5 and poor with 0-2 (Cooper et al.) [11]

All patients were monitored intraoperatively. Data noted included onset time of intubation, intubating conditions at the time of intubation, heart rate, mean arterial blood pressure and oxygen saturation. The above data were recorded at baseline, immediately after intubation, 1 min and 5 min after endotracheal intubation.

Statistical analysis

Descriptive statistics for continuous variables such as age, weight and onset time of intubation were presented as mean and standard deviation while the inferential statistics for hypothesis testing were performed with unpaired "t" test. Categorical data were compared using the Chi-square test. Graphical representation was presented by bar diagrams and statistical analysis was performed using SPSS 20.0 statistical package. Statistical significance was considered if $p < 0.05$.

RESULTS

There were no significant differences comparable in both the groups with respect to age, weight, sex, ASA physical status and Mallampati grading. The mean age in group A was 45.35 ± 13.74 yrs. and in group B was 45.00 ± 12.65 yrs (Table 1). The mean weight in group A was 54.50 ± 7.14 kg and in group B was 56.13 ± 5.60 kg (Table 1). The number of male and female patients in Group A are 23 and 17 respectively and in Group B are 20 and 20 respectively (Table 1). The number of ASA physical status 1 and 2 patients in Group A are 17 and 23 respectively and in Group B are 17 and 23 respectively (Table 1). The number of Mallampati grade 1 and 2 patients in Group A are 14 and 26 respectively and in Group B are 20 and 20 respectively (Table 1).

The Intubation score was 8–9 in both the groups,which comes under the excellent grade of Cooper'sscore. The intubation score was recorded in two groupsafter loss of T1 response of TOF. The onset time of intubation was 60 ± 10.17 sec in group A compared with 38.7 ± 8.80 sec in group Bwith p value <0.001 which is statistically significant.(Table 1).

Table 1: Demographic data and onset time of intubation

Variables	Group A	Group B	P
Age (yrs)	45.35 ± 13.74	45.00 ± 12.65	0.906
Weight (kg)	54.50 ± 7.14	56.13 ± 5.60	0.261
Sex (Male/Female)	23/17	20/20	0.501
ASA PS(1/2)	17/23	17/23	1.000
Mallampati grade (I/II)	14/26	20/20	0.175
Onset time of intubation	60 ± 10.17	38.7 ± 8.80	< 0.001

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Table 2: Variation in HR in each group

Variables	Group	N	Mean HR	Std. Deviation
Baseline HR	A	40	75.40	11.01
	B	40	76.725	8.69
HR immediate intubation	A	40	77.00	10.29
	B	40	79.275	9.78
HR at 1 min	A	40	74.125	9.73
	B	40	75.70	9.76
HR at 5 min	A	40	72.525	9.78
	B	40	73.80	9.92

Table 3: Variation in MAP in each group

Variables	Group	N	Mean MAP (mmHg)	Std. Deviation (mmHg)
Baseline MAP	A	40	98.875	10.10
	B	40	96.375	7.90
MAP immediate intubation	A	40	97.15	7.75
	B	40	95.875	8.11
MAP at 1 min	A	40	94.35	8.66
	B	40	93.85	7.49
MAP at 5 min	A	40	91.65	8.11
	B	40	91.45	8.59

The mean baseline HR in Group A and B are 75.40 (±11.01) and 76.725 (±8.69) respectively, mean HR immediate intubation in Group A and B are 77.00 (±10.29) and 79.125 (±9.78) respectively, mean HR at 1 min in Group A and B are 74.125 (±9.73) and 75.70 (±9.76) respectively and mean HR at 5 min in Group A and B are 72.525 (±9.78) and 73.80 (±9.92) respectively (Table 2). The mean baseline MAP in Group A and B are 98.875 mmHg (±10.10) and 96.375 mmHg (±7.90) respectively, mean MAP immediate intubation in Group A and B are 97.15 mmHg (±7.75) and 95.875 mmHg (±8.11) respectively, mean MAP at 1 min in Group A and B are 94.35 mmHg (±8.66) and 93.85 mmHg (±7.49) respectively and mean MAP at 5 min in Group A and B are 91.65 mmHg (±8.11) and 91.45 mmHg (±8.59) respectively (Table 3)

The heartrate wasincreased at immediately after intubation and this heightened response could be due to stress response to endotracheal intubation.

DISCUSSION

In our study, using 2.3 × ED_{95} dose of rocuronium showed that with priming (priming with 10% of the intubating dose with 3 min priming interval), the onset time of intubation (onset of maximum block) was 38.7 ± 8.80 sec in the priming group and 60 ± 10.17 sec in the control group (Table 1) with comparable intubating conditions in both groups at the time of intubation, i.e. after loss of T1 of TOF

Raoet al. [12] had compared priming with non-priming of rocuronium by giving a priming dose of 0.06mg/kg of rocuronium followed by 0.54mg/kg 3 min later and another group directly 0.6mg/kg of rocuronium. Onset times were compared in both the groups which were 50.67 ± 7.39 sec with priming and 94 ± 11.626 sec without priming. The intubating conditions were excellent in both the groups

Griffith et al. [13] also had compared priming with non-priming of rocuronium by giving dose of 0.06mg/kg rocuronium followed by 0.54mg/kg 2 min later and another group given directly 0.6mg/kg rocuronium. Onset times were compared in both the group which were 34 ± 6 sec with priming and 59 ± 14 sec without priming

In our study, none of the patients developed any adverse effects of priming. The subtle symptoms of adverse effects of priming could not have been felt due to the premedication with midazolam and fentanyl before the priming dose.

The major drawbacks of priming dose is the occurrence of adverse effects such as weakness, diplopia, dysphagia generalized discomfort and comfort and breathing difficulties. Aziz et al. [14] had explained the effects of priming with vecuronium and rocuronium in younger and elderly patients. Totally 10 patients in each group in young and elderly were selected in both rocuronium and vecuronium groups. 7 younger patients in vecuronium and 6 in rocuronium groups developed ptosis. 5 younger patients in vecuronium and 4 in rocuronium groups developed difficulty in swallowing, expiratory reserve volume was reduced by 20-25% and oxygen saturation was decreased. Decrease was minimal in younger patients compared with the elderly. 8 elderly patients in vecuronium and 7 in rocuronium groups developed ptosis, 5 elderly patients in vecuronium and 4 in rocuronium groups developed difficulty in swallowing expiratory reserve volume reduced by 30-40% and oxygen saturation was decreased. Decrease was higher in elderly patients than in younger patients.

The autonomic safety ratio of rocuronium for vagal block is about 10 times less than that of vecuronium. No haemodynamic changes (blood pressure, heart rate) were seen. Slight to moderate increase in heart rate may be because either the rocuronium produces pain on injection or to its weak vagolytic effect. It may be controlled by the prior administration of fentanyl [15]

In our study, any increase in heart rate or blood pressure after rocuronium administration was not observed and this may be due to prior administration of midazolam and fentanyl. Slight increase in heart rate immediately post intubation (Table 1) was observed which may be due to stress response to intubation.

Heier et al. [16] gave midazolam 0.01mg/kg, alfentanil 10µg/kg and thiopentone 4mg/kg. It was then followed by various doses of rocuronium for rapid sequence induction and intubation. The cardiovascular changes with doses of rocuronium with intubating doses of 0.4, 0.8, 1.2, 1.6 and 2 mg/kg and thereafter percentage change in BP were 30, 24, 29, 22 and 17 respectively and percentage change in heart rate were 7, 8, 7, 7 and 5 respectively.

Various studies comparing rocuronium and succinylcholine in the onset time and quality of intubation have yielded varying results. McCourt et al. [17] have found that rocuronium 1mg/kg and succinylcholine 1mg/kg have shown excellent intubating conditions at 60 sec. Singh et al. [18] shown that with 0.6mg/kg rocuronium and 1.5mg/kg succinylcholine, the time to achieve maximum blockade was 87.94 and 65.59 sec respectively. The intubating conditions were comparable in both the groups at 60 sec.

Naguib et al. [19] had given the priming dose as 0.06 mg/kg rocuronium or 0.015mg/kg mivacurium followed by 0.54mg/kg of rocuronium. Priming with rocuronium and mivacurium, the onset times were 73 and 58 sec respectively and in the other group, succinylcholine 1mg/kg was administered and the onset time was found to be 54 sec. Intubating conditions were found to be similar in all three groups. It was then concluded that priming rocuronium with either rocuronium or mivacurium resulted in neuromuscular blockade comparable to that of succinylcholine in both the onset of action and intubating condition.

Jose et al. [20] have found that the priming interval of 4 min allowed the faster onset time compared with the 2 and 6 min priming intervals. Yavascaoglu et al [21] has proved that 3 min priming interval was more effective than the 2 min when RSI with rocuronium was necessary. Foldes et al. [22] have not observed any improvement in the onset times when rocuronium 0.1mg/kg followed by 0.5mg/kg 4 min later was administered. Taboada et al. [23] had reported that if priming interval is increased it will result in shortened onset time of the intubating dose. However, increasing the priming interval beyond the “optimal” interval will result in prolonging the onset of the intubating dose.

CONCLUSION

In clinical conditions where rapid sequence induction is required and contraindication of succinylcholine coexist, due to its own adverse effects, rocuronium with priming principle can be safely used with similar intubating conditions. It is also useful where prolonged duration of action by the application of a mega dose of rocuronium is not desired. Therefore, rocuronium with priming principle can be a safe alternative to succinylcholine for rapid sequence intubation. However, priming should be performed cautiously and the patient monitored closely

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