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Comparative Evaluation of Intubating Conditions and Haemodynamic Effects after the Administration of Succinylcholine and Rocuronium Bromide.

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Conflicts of Interest: Nil

Abstract

Background: Suxamethonium has been the gold standard depolarizing muscle relaxant for rapid sequence enotracheal intubation. Due to its many side effects, like, muscular fasciculations, bradycardia, dysrhythmia, hyperkalemia, rise in intra ocular, intracranial and intrgastric pressure, incidence of prolong recovery in patients with pseudocholinestarase deficiency and malignant hyperthermia, alternative of suxamethonium are being studied. Rocuronium, an intermediate acting non-depolarizing muscle relaxant, is being studied as an alternative to suxamethonium for endotracheal intubation beacause of its lesser side effects.

Aims and objectives: Observe and compare the intubating conditions, onset of time, duration of action & haemodynamic effect in patients receiving succinylcholine and rocuronium bromide in different doses for rapid tracheal intubations.

Methods: Sixty patients were divided in three groups according to the muscle relaxant used for endotracheal intubation for general anesthesia for elective surgeries: Group I Patients (n=20) received succinylcholine chloride 1.5 mg/kg intravenous (IV), group II Patients (n=20) received rocuronium Bromide 0.6 mg/kg IV and group III Patients (n=20) received rocuronium Bromide 0.9 mg/kg IV. Peripheral nerve stimulator was used to monitor the effect of muscle relaxants. Onset time and duration of action of the muscle relaxant, intubating condition, time to intubate and hemodynamic parameters were recorded. Data compared statistically.

Results: The mean onset time for group I was 45.5 (±8.87) seconds, for group II was 87.5 (± 13.32) seconds and for group III was 70 (±16.88) seconds and was statistically significant between the three groups. Clinical duration of intubating dose of 0.6 mg/kg rocuronium was significantly lesser than that of rocuronium 0.9 mg/kg (35.68 ± 3.84 minutes vs 53.65 ±4.18 minutes, $p<0.01$). The intubating conditions were graded as excellent in 19 (95%), 12 (60%) and 18 (90%) patients of group I, II and III respectively. Heart rate and mean arterial pressure remained statistically insignificant between the groups.

Conclusion: rocuronium is not a remedy for all intubation nor a replacement for traditional succinylcholine but there is growing body of evidence that suggest its equivalence to or superiority over conventional succinylcholine.

Key words: Rocuronium, Succinylcholine, Endotracheal intubation, Muscle relaxants

Introduction

Today endotracheal intubation is an integral part of administration of general anaesthesia during surgical

procedures to maintain airway, to allow intermittent positive pressure ventilation and to prevent aspiration. Dangerous period for aspiration is the time interval between suppression of protective reflexes & development of satisfactory intubating conditions. Hence this time interval should be as short as possible.

Succinylcholine introduced by the Daniel Bovet et al in 1949, revolutionized anaesthetic practice by providing intense neuromuscular blockage of very rapid onset and ultra-short duration of action, and is still relaxant of choice for routine intubation and rapid sequence induction of anaesthesia [1]. But in addition to fasciculations it has got many side effects such as bradycardia, dysrhythmia, hyperkalemia, rise in intra ocular pressure, increase intra cranial pressure, increase intra gastric pressure, post op myalgia, incidence of prolong recovery in patients with pseudocholinestarase deficiency and malignant hyperthermia.

Therefore the search is on for agent, which has a non-depolarizing mechanism of action, rapid onset of action, rapid recovery, non-cumulative effect, without cardiovascular side effects, with high potency, pharmacologically inactive metabolites, and reversibility with cholinesterase inhibitors.

Recently developed neuromuscular blocking drugs are of intermediate duration and to a major extent free of side effects. However, even after intubating doses, onset of action is relatively slow as compared to succinylcholine. Among the muscle relaxants in current use the intermediate acting non-depolarizing muscle relaxants-rocuronium bromide is a newer aminosteriod neuro-muscular blocking agent related to vecuronium bromide but has a greater lipophilicity, lesser potency and a very fast onset of action [2]. Several clinical studies conducted by various workers have confirmed the brief onset time of rocuronium bromide [3-5]. The purpose of the present study is to observe and compare the intubating conditions, onset of time, duration of action & haemodynamic effects in ASA grade I/II receiving succinylcholine & rocuronium bromide in different doses for rapid tracheal intubations.

Material and Methods

After obtaining institutional ethical committee clearance and informed written consent for surgery and general anaesthesia 60 patients of ASA grade I and II, aged between 20 to 60 years, undergoing various surgical procedures were selected for the study. All patients underwent a thorough preanaesthetic check up. Patients with renal disease, hepatic disease, cardio vascular and respiratory problems and patient with anticipated airway difficulty were not included in study.

Patients were divided in 3 groups. Group I Patients (n=20) received succinylcholine chloride 1.5 mg/kg intravenous (IV), group II Patients (n=20) received rocuronium Bromide 0.6 mg/kg IV and group III Patients (n=20) received rocuronium Bromide 0.9 mg/kg IV for Tracheal Intubation.

All patients received diazepam 0.1 mg/kg the night before surgery. On arrival to the operating room, an IV access was established and monitors for heart rate, electrocardiography, blood pressure and arterial oxygen saturation were attached & vital parameters were recorded. Surface electrodes of neuromuscular monitor were applied to forearm at wrist to stimulate ulnar nerve.

Patients were premedicated with glycopyrolate 4 µg/kg IV and fentanyl 2µg/kg IV 15 min. before induction. After Pre-oxygenation for 3 minutes, anaesthesia was induced with thiopentone 5-7 mg/kg IV till the loss of eye lashes reflex. Before administration of muscle relaxant, the supramaximal stimulus was determined with the help of the peripheral nerve stimulation by observing contraction of adductor pollicis by visual, tactile assessment. After induction, muscle relaxant according to

the group given in fast running IV line. After giving muscle relaxant the single twitch stimulus was given every 10 seconds, the time interval from end of injection of muscle relaxant to maximum suppression of control twitch height (onset time) was noted.

An experienced anaesthesiologist, unaware about the muscle relaxant, performed endotracheal intubation. Intubation attempt was made at 60 seconds after administration of the muscle relaxant. Intubating condition were assessed as excellent, good, fair or poor based on jaw relaxation, position and movement of vocal cords and diaphragmatic response to intubation using Copenhagen consensus conference rating scale (Table 1). If the intubation conditions assessed, not found satisfactory, the intubation was stopped and subsequent attempts were made at 30 seconds interval until intubation was achieved with acceptable intubating conditions.

Time duration of intubation after muscle relaxant noted at : 60 sec / 90 sec / 120 seconds.

Anaesthesia was maintained with 40% O_2 + 60% N_2O supplemented with isoflurane 0.5-1% and rocuronium infusion with controlled ventilation. The neuromuscular block was observed by using the Train-of-Four (TOF) response at 12 seconds interval. At spontaneous T1 recovery of approximate 25% of control (after intubating dose), rocuronium infusion was started in a dose of 0.3 mg/kg/hr and rate was adjusted to maintain 1 to 2 response to TOF stimuli, if required. The time from administration of muscle relaxant to 25% recovery (Duration of Action) was recorded. Rocuronium infusion was stopped 15-20 minutes prior to expected end of surgery. At the completion of surgery neuromuscular block was reversed by using neostigmine 0.05 mg/kg IV and glycopyrolate 0.008 mg/kg IV. The extubation was performed when the patient was fully awake and T1 returned to approximately 90% of control. The patient was monitored for 24 hrs in post operative period for a residual muscle Paralysis. Any adverse cardiovascular event or allergic reaction to the drug used was noted.

At the end of the study, data collected were statistically compared using student 't' test.

Results

We have studied 60 ASA grade I/II patients undergoing various elective surgeries with 20 patients in each group. Demographic data were comparable between the three groups (Table 2).

The mean onset time for group I was 45.5 (±8.87) seconds, for group II was 87.5 (± 13.32) seconds and for group III was 70 (±16.88) seconds (Table 3). The difference between the groups I and II was statistically highly significant ($p<0.01$). Difference between group II and III was statistically significant ($p<0.02$). But the difference between group I & III was statistically highly significant ($p<0.01$).

Clinical duration of intubating dose of succinylcholine 1.5 mg/kg was the shortest among the three groups (Table 3). Clinical duration of intubating dose of 0.6 mg/kg rocuronium was significantly lesser than that of rocuronium 0.9 mg/kg (35.68 ± 3.84 minutes vs 53.65 ±4.18 minutes, $p<0.01$).

The intubating conditions were graded as excellent in 19 (95%), 12 (60%) and 18 (90%) patients of group I, II and III respectively (Table 4). The difference was statistically significant between group I and II ($p<0.05$) and group II and III ($p<0.05$) but not significant between group I and III ($p>0.05$). Good intubating conditions were seen in 1 (5%), 8 (40%) and 2 (10%) Patients of group I, II and III respectively and was statistically significant between the groups I and II ($p < 0.05$). Difference between groups II and III was not significant statistically ($p>0.05$).

With intubating dose of succinylcholine (1.5 mg/kg) and rocuronium (0.9 mg/kg) all patients could be intubated at

60 seconds (Table 5). While with intubating dose of rocuronium (0.6 mg/kg) 10 (50%) patients could be intubated at 60 seconds and 10 (50%) patients at 90 seconds.

After anesthesia induction and administration of muscle relaxant heart rate (HR) increased from base line in 11(55%) patients in group I, 13 (65%) patients in group II and 20 (100%) patients in group III (Table 6). Of those patients who did not show this tachycardia response (7 in group I and 3 in group II) the decrease in HR was less than 10% in all patients but one patient in group I showed decrease in HR > 10% .Two (10%) patients in group I and 4 (20%) patients in group II did not show any change in HR. while increase in HR noted in 3 (15%) patients in group III. Maximum rise in mean arterial pressure (MAP) seen at or just after intubation (Table 7). MAP returned to basal value after 5 minutes of intubation. However the difference in MAP after relaxant in all the 3 groups were clinically and statistically insignificant (table 9).

Discussion

Initial studies showed that rocuronium, being a low potency compound was associated with a rapid onset of effect when compared with other compounds such as vecuronium and mivacurium [6, 7]. This has seen been demonstrated in many clinical studies that the onset of action of rocuronium is significantly faster when compared to equipotent doses of vecuronium, although slightly slower than that of succinylcholine [8,9].

Initial studies in animal's demonstrated rocuronium to be 10-20% as potent as vecuronium and ED doses were found to be from 0.26 mg/kg to 0.30 mg/kg. Intubating dose of rocuronium used in this study are 0.6 mg/kg and 0.9 mg/kg.

Use of higher dose of rocuronium to improve intubating conditions during rapid sequence intubation and to cut short the onset time below 60 seconds has been advocated by various workers but doses larger than 0.6 mg/kg would be associated with a long duration of action which may be inappropriate for surgeries of short duration [10].

In most studies, an appropriate timing of tracheal intubation has been determined by 3 ways; 1.Clinical Judgement, 2. Neuromuscular monitoring either by Twitch suppression (maximum blockade) or TOF ratio and 3. Predetermined time after the administration of neuromuscular blocking Agent.

The technique using judgment alone is relatively insensitive. Onset time differs with different nerve stimulation rates used. Cooper et al found onset time for rocuronium 0.6 mg/kg as 90 seconds by 0.1 Hz stimulation and 58 seconds using TOF stimulation [11]. Alternatively, a predetermined time for tracheal intubation can be used. In present study we have used all the 3 parameters.

Land et al were probably the first to introduce a rating scale as a tool for the assessment of intubating conditions in which the three main criteria: Jaw relaxation, vocal cords (position and motility) and reaction to intubation were rated by descriptive scores such as excellent, satisfactory and fair [12]. These three main criteria remained the basis of numerous subsequent modification of their rating scale by others. Modification of this rating scale, Copenhagen consensus conference rating scale was used in the present study.

Data of our study shows that there is not an appreciable difference in the intubating conditions after the administration of either rocuronium 0.9 mg/kg or succinylcholine 1.5 mg/kg. The clinically acceptable conditions are present in all the patients in the three groups receiving succinylcholine 1.5 mg/kg, rocuronium 0.6 mg/kg and rocuronium 0.9 mg/kg respectively, but in group II (rocuronium 0.6 mg/kg) only 12(60%) patients showed excellent intubating conditions, while 19(95%)

patients of group I (succinylcholine 1.5 mg/kg) and 18(90%) of group III (rocuronium 0.9 mg/kg) showed excellent intubating conditions. Similar results were found in the studies carried out by, Wierda J et al , Cooper et al, Zhou et al, and Weiss JH et al [6, 11, 13, 14].

In a study conducted by Mc Court K C et al the intubating conditions after 0.9 mg/kg rocuronium appeard to be practically identical to those observed after 1.0 mg/kg succinylcholine (96% vs 97%) for clinically acceptable intubating conditions [4].

Sparr et al and Crul et al, investigated rocuronium's potential in emergency intubating conditions using it strictly according to the scenario for rapid sequence induction in unpremedicated but still elective cases [15, 16]. In those studies, the frequency distribution of 'excellent', 'good', or clinically acceptable intubating conditions, 60 seconds after 0.6 mg/kg or 0.9 mg/kg rocuronium were compared with those observed after 1.0 mg/kg succinylcholine. The results indicate that intubating conditions were more favourable at 60 sec after administration of rocuronium in the dose of 0.9 mg/kg compared to dose of 0.6 mg/kg in unpremedicated patients.

Similar results about onset time and intubating conditions were found in another study of Bhardwaj N. et al [17]. In their study no difference was observed in the frequency distribution of clinically acceptable intubating conditions at 60 seconds after the administration of succinylcholine (1.5 mg/kg) or rocuronium (0.9 mg/kg), but clinically acceptable intubating conditions at 60 seconds were obtained in only 37% in rocuronium 0.6 mg/kg group.

In a study by cooper et al, they found the onset time of 88.90 seconds and 60.40 seconds for rocuronium 0.6 mg/kg and succinylcholine 1.0 mg/kg, respectively [11]. In another study conducted by Puhringer et al, they noted the onset time as 72.0 seconds & 48.0 seconds for rocuronium 0.6 mg/kg and succinylcholine 1.0 mg/kg, respectively [18].

The time to achieve maximum block of approximately 88.5 seconds with rocuronium 0.6 mg/kg and 70 seconds with rocuronium 0.9 mg/kg was significantly longer than a time of about 45.5 seconds with succinylcholine 1.5 mg/kg in the present study and is in accordance with the finding of other authors.

Magorian et al compared the onset time and duration of action of rocuronium in doses of 0.6 mg/kg, 0.9 mg/kg and 1.2 mg/kg with that of succinylcholine in the dose of 1.0 mg/kg [19]. They were found onset time to be 89 seconds, 75 seconds, 55 seconds, and 50 seconds respectively. Duration of action was found to be 37 minutes, 53 minutes, 73 minutes and 9 minutes respectively. In our study duration of action of rocuronium 0.6 mg/kg, rocuronium 0.9 mg/kg and succinylcholine 1.5 mg/kg are 35.68 minutes, 53.65 minutes and 7.9 minutes respectively and in accordance with prior studies.

There were no significant changes in HR and MAP after the administration of muscle relaxant in either of group in the study. The small rise in HR and decrease in MAP after induction and muscle relaxant may be due to cardiovascular effects of induction dose of thiopentone. The studies conducted by Nitschmann et al, Cooper et al and Levy et al show similar cardiovascular effects [8, 11, 20].

Before the introduction of rocuronium, vecuronium was the only non-depolarizing agent available for the use in haemodynamically unstable patients. Use of vecuronium in gynecological and squint surgery is sometimes associated with sudden bradycardia. In these patients rocuronium can be used safely as it does not cause bradycardia rather it causes slight tachycardia which is not significant clinically. As there is no significant change in

HR and MAP with rocuronium, it is agent of choice in cardiac and other haemodynamically unstable patients.

There were no intra oprative and post porative complications in all the groups.

Conclusion

We conclude that rocuronium, a newer nondepolarizing muscle relaxant with a brief onset of action and intermediate duration, but devoid of the adverse reactions associated with succinylcholine may be a suitable alternative to succinylcholine for tracheal intubation. However, 90 seconds are required with rocuronium 0.6 mg/kg to achieve clinically acceptable intubating conditions. Rocuronium in a dose of 0.9 mg/kg may be valuable alternative to succinylcholine for rapid tracheal intubation in emergency situations where succinylcholine is contraindicated and surgery is of intermediate duration. Thus, though rocuronium is not a remedy for all intubation nor a replacement for traditional succinylcholine but there is growing body of evidence that suggest its equivalence to or superiority over conventional succinylcholine.

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List of Tables

Table 1.COPENHAGEN CONSENSUS CONFERENCE RATING SCALE

INTUBATING CONDITIONS	CLINICALLY ACCEPTABLE		CLINICALLY UNACCEPTABLE
Variables	Excellent	Good	Poor
1. Laryngoscopy	Easy	Fair	Difficult
2.Vocal Cords			
• Position	Abducted	Intermediate	Closed
• Movements	None	Moving	Closing
3. Reaction to Intubations			
• Movements of Limb	None	Slight	Vigorous
• Coughing	None	Diaphragm	Sustained (>10s)

Table 2. Demographic data (Mean ± SD).

	Group-I (n=20)	Group-II (n=20)	Group-III (n=20)
Age	40.85 ± 14.53	42.60 ± 10.95	45.90 ± 10.15
Body Weight.	61.90 ± 10.78	57.40 ± 07.58	60.50 ± 11.25
Male: Female	9:11	9:11	11:9

Table-3: Onset Time / Duration Of Action (Mean ± SD)

	Group-I	Group-II	Group-III
Onset Time (sec)	45.50 ± 08.87	87.50 ± 13.32	70.00 ± 08.88
Duration Of Action (min)	07.90 ± 00.78	35.68 ± 03.84	53.65 ± 04.18

Table -4: Intubating Conditions

	Group-I (n=20)		Group-II (n=20)		Group-III (n=20)	
Intubating conditions	No. of Pts.	%	No. of Pts.	%	No. of Pts.	%
Excellent	19	95%	12	60%	18	90%
Good	1	5%	8	40%	2	10%
Fair						
Poor						

Table-5: Intubation Time

Time (seconds)	Group-I (n=20)	Group-II (n=20)	Group-III (n=20)
60 sec	20	10	20
90 sec	-	10	-
120 sec			

Table-6: Changes In Pulse Rate / minute (Mean ± SD)

Time	Group – I	Group – II	Group – III
Basal	81.75 ± 10.57	82.85 ± 09.08	79.80 ± 06.45
After Relaxant	82.40 ± 08.23	85.40 ± 11.21	86.65 ± 06.18
After Intubation	91.25 ± 10.04	98.55 ± 09.54	97.95 ± 06.47
1 min after intubation	88.75 ± 09.57	92.20 ± 09.24	86.80 ± 06.36
2 min after intubation	87.40 ± 08.43	90.85 ± 08.74	86.05 ± 06.04
3 min after intubation	86.15 ± 07.88	89.50 ± 09.26	84.10 ± 07.10
4 min after intubation	84.70 ± 08.56	89.90 ± 10.00	82.40 ± 06.45
5 min after intubation	83.20 ± 10.87	84.00 ± 07.58	82.20 ± 05.70

Table-7: Changes In Mean Arterial Pressure (Mean ± SD mm of Hg)

Time	Group - I	Group - II	Group – III
Basal	96.65 ± 05.72	89.35 ± 02.25	91.30 ± 03.96
After Relaxant	92.15 ± 06.84	89.85 ± 02.79	89.20 ± 04.45
After Intubation	100.70 ± 09.07	96.60 ± 04.07	95.40 ± 03.35
1 min after intubation	97.55 ± 04.24	92.75 ± 03.48	93.15 ± 04.68
2 min after intubation	94.60 ± 04.21	91.60 ± 03.63	90.15 ± 03.37
3 min after intubation	93.00 ± 04.30	90.15 ± 03.20	87.85 ± 04.43
4 min after intubation	91.15 ± 05.13	89.15 ± 03.97	86.45 ± 04.03
5 min after intubation	90.75 ± 05.59	89.95 ± 03.44	86.40 ± 04.27