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Comparison between Intubating and Recovery Characteristics of Succinylcholine, Rocuronium and Atracurium in Parturients Undergoing Cesarean Sections.

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Abstract: Woman undergone general anesthesia for caesarean section, need a rapid sequence induction to protect against pulmonary aspiration. Succinylcholine is the most commonly used muscle relaxant due to its fast onset and short duration but it has many serious complications. Rocuronium a new muscle relaxant with a brief onset of action, but devoid of the succinylcholine adverse effects may be a suitable alternative to it and to test this hypothesis, the intubating and recovery characteristic of succinyl choline, recuronium and atracurium were compared. This study was conducted on 60 parturients delivered by elective cesarean section. Aged 18 to 37 years and physical status ASA I and II. They were divided into 3 groups: group I was given 0.6 mg. kg-1 rocuronium (n = 20), group II was given 0.5 mg. kg-1 atracurium (n = 20) and group III was given 1 mg. kg-1 succinylcholine (n = 20). The intubation conditions were assessed. heart rate and mean arterial blood pressure were monitored before induction of general anesthesia after induction of general anesthesia and then at 1, 3, 5, 10, 15 and 20 minutes after muscle relaxant administration then every 10 minutes. Subjective TOF ratio was recorded at 0, 1, 2 and 3 minutes from injection of the muscle relaxant and then every 5 minutes until reverse. The onset time, the clinical duration of action of the muscle relaxants, recovery time and recovery index were recorded. The main results of the present study were as follow: Rocuronium gave good and excellent intubating conditions at 60 seconds significantly higher than atracurium and comparable to intubation at 60 seconds following succinylcholine. Rocuronium had significantly shorter onset time and clinical duration than atracurium and had rapid onset of action approaching that of succinylcholine. It had significantly shorter recovery time than atracurium and had significantly lower number of patients with fade in TOF at 1 minute post its injection than atracurium. Number of patients with zero fade in TOF at 1 minute post injection of rocuronium was significantly higher than atracurium. Rocuronium had significantly lower number of patients with no fade in TOF at 60 minutes post injection of NDMR than atracurium.

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1. Introduction.

Cesarean sections are performed under regional or general anesthesia but the general anesthesia for cesarean section is still decreasing in incidence. The Potential problems associated with general anesthesia for cesarean section include failed intubation, pulmonary aspiration of gastric contents, neonatal depression and maternal awareness ***(Miller, R. D et al., 2010).***

Rapid sequence induction and intubation (RSII) is an anesthesia induction method designed to facilitate rapid tracheal intubation in patients at high risk of aspiration. The main objective of the technique is to minimize the time interval between loss of protective airway reflexes and tracheal intubation with a cuffed endotracheal tube ***(El-Orbany, Mohammad et al., 2010)***. This method consists of the positioning of the patient, pre-oxygenation, rapid injection of the dose of the hypnotic, followed by the rapid acting neuromuscular blocker, pressure on the cricoid cartilage, avoiding positive pressure ventilation (PPV) before the tracheal intubation with the balloon tube ***(Guirro, Ursula Bueno do Prado et al., 2012).***

Muscle relaxants are given as part of a rapid-sequence induction to facilitate tracheal intubation. Among all the muscle relaxants available, succinylcholine is the only one with a fast onset and a fast recovery. So it is still the most frequently used muscle relaxant for rapid-sequence induction despite its well-known side-effects ***(Sparr HJ, 2001).***

Succinylcholine is a depolarizing muscle relaxant that can cause hyperkalaemia, muscle pains, bradycardia and malignant hyperpyrexia. It has a high incidence of anaphylaxis and histamine release.

Raised intraocular, intracranial and intragastric pressure may occur with resultant passive regurgitation in the presence of an incompetent lower oesophageal sphincter ***(Sinclair, Rhona CF et al., 2005)***. Due to Succinylcholine side effects any an equally effective muscle relaxant without these side effects would be advantageous. Because most of its side effects reflect its depolarizing mechanism of action thus search for ideal neuromuscular blocking agent focused on nondepolarising type of relaxants which has rapid onset time and offers good to excellent intubation conditions, as rapidly as suxamethonium and which lacks the above mentioned side effects ***(Ajeet, Singh et al., 2004).***

Rocuronium bromide is a non depolarizing muscle relaxant being used for tracheal intubation and can be reversed by a specific antidote. some suggested that is replacing succinylcholine for intubating parturient women (***Sudha, P et al., 2016)***. However, atracuriumbesylate despite its long onset is frequently used for that purpose in a real life practice in Egypt. The present study compares the intubating and recovery characteristic of succinylcholine recuronium and atracuriumin parturient undergoing general anesthesia for caesarean section .

Aim Of The Work.

This study aimed at comparing the onset and recovery times, hemodynamic changes, tracheal intubation conditions and recovery characteristic of succinylcholine, rocuronium and atracurium in parturients undergoing general anesthesia for elective caesarean sections.

2. Patients and Method.

After obtaining approval from the Ain Shams University Research Ethics Committee and informed consent from the patients, 60 parturient undergoing cesarean section were included, aged 18 to 37 years and physical status ASA I and II.

Type of Study: A prospective, randomized double-blinded clinical study.

Study Setting: Obstetrics and delivery unit at Ain Shams University Hospital in Cairo.

Study Period: Six months from June 2018 to November 2018 .

Study Population: Parturients scheduled for elective caesarean section under general anesthesia aged 18-37 years.

Inclusion Criteria: .

- Patients ASA physical status I-II.
- Patients 18-37 years.
- Patients having given informed consent to the study.

Exclusion Criteria:.

- Known or suspected allergy towards the used anesthetics or the muscle relaxant .
- Known or suspected neuromuscular disease (Multiple sclerosis, myasthenia gravis).
- Anatomic and functional malformations with expected difficult intubation.
- Body mass index >35kg/$m^{2.}$
- Contraindication for the use of rocuronium, atracurium or suxumethonium.
- History of malignant hyperthermia in relatives.

Sampling Method: Simple Random Sampling using a computer program.

Sample Size: 60 parturients.

Med Calc® version 12.3.0.0 program "Ostend, Belgium" was used for calculations of sample size. Statistical calculator based on 95% confidence interval and power of the study 80% with α error 5%, based on the study of Chavan et al, sample size was calculated to be a minimum of 57 cases. Assuming a drop-out ratio of 5%, the sample size will be 60 cases, subdivided into three groups, 20 cases in each group ***(Chavan et al., 2016).***

Preoperative preparation:.

1- Full medical history and examination was done including:.

a- History of any previous disease as cardiac, respiratory, renal, hepatic and neuromuscular disease.

b- General examination .

c- Airway assessment to exclude cases with anticipated airway difficulty.

d- Patients' weights were recorded .

e- Preoperative heart rate and mean ABP were recorded.

2- Routine laboratory investigations was done which included: liver function tests (alkaline phosphatase, alanine transaminase, aspartate aminotransferase and total bilirubin), kidney function tests (serum creatinine & blood urea nitrogen), complete blood picture, coagulation profile (Prothrombin time, activated partial thromboplastic time & international normalized ratio), fasting blood sugar.

3- Premedication with 0.3 %Molar Sodium Citrate 30 ml orally 30 minutes before operation.

Positioning:

The patients were placed in supine position with head up 20°. Left uterine displacement was done using a wedge under the right hip. Patients' forearms were extended on arm rests with palm facing upwards. One hand was used for the insertion of 18 G cannula, pulse oximeter and NIBP monitoring. The other was used for neuromuscular transmission monitoring using a peripheral nerve stimulator.

Grouping:

According to the muscle relaxant used, patients were allocated randomly to receive one of the following drugs: group1(**GI)** was given 0.6 mg. kg^{-}

[1]rocuronium after propofol injection (20 Patients); group II (**GII**) was given 0.5 mg. kg^{-1} atracurium just before propofol injection (20 Patients); group III (**GIII**) (control group) was given 1 mg. kg^{-1} succinylcholine after propofol injection (20 Patients).

Induction of Anesthesia.

After preoxygenation with 100 % oxygen was given until end expired oxygen concentration of ≥80%, anesthesia was induced with 2 mg. kg-1 propofol followed by succinylcholine, rocuronium or atracurium just before propofol injection. Neuromuscular blocking agents were injected over 5 seconds. Volume controlled mechanical ventilation was done when apnea occurred using TV 6-8 ml. kg^{-1}, I: E ratio 1:2 respiratory rate 12-14 /minute and zero PEEP until after securing the ETT and inflation of the cuff until after a 5 cm H2O PEEP was applied.

Sixty seconds after the end of the injection of muscle relaxant, the trachea was intubated in all patients by the same experienced anesthetist who was blinded to patient's grouping by physical screen at cannula site and he assessed intubating conditions using the following criteria: Excellent: jaw relaxed vocal cords abducted and immobile and no diaphragmatic movement. Good: jaw relaxed vocal cords abducted and immobile and some diaphragmatic movement. Poor: jaw relaxed, vocal cords moving, and coughing or bucking. Inadequate: jaw not relaxed and vocal cords closed ***(Fuchs-Buder et al 1996).***

Cricoid pressure was applied from loss of consciousness till confirmation of proper endotracheal tube insertion by auscultation and capnography and inflation of cuff.

Before any muscle relaxant is administered, the mechanical evoked response of adductor pollicis muscle to the first stimulus (T1) in train of four sequence was determined and for supramaximal stimulation (SMS). Patients were given 30 mg propofol to reduce nerve stimulator pain then single twitch stimulation at 1 HZ and 70 m A was applied with a Micro stim (Sun. Med. inc. Clearwater, FL, UA) peripheral nerve stimulator. Once the control response was gained, the remains of propofol dose was given as well as the muscle relaxant is administered. A "Micro stim "peripheral nerve stimulator delivered supramaximal square wave impulse of 0.2 ms duration and 70 m A in train of four sequence (2 HZ) via surface electrode placed near the ulnar nerve at the wrist (fig.9).

TOF ratio (visual /tactile TOF ratio) was recorded at 0, 1, 2 and 3 minutes from injection of the muscle relaxant and then every 5 minutes until reversal of muscle relaxant.

The force of contraction of the fourth muscle twitch was visually and tactilely compared to the contraction of the first twitch by feeling the strength of contraction of muscles and assessing TOF fade (tactile means) and fade was considered absent (no fade) when both muscle contractions (twitches) appear equal (no block). When the fourth twitch in the TOF sequence started decreasing in amplitude, the TOF ratio became less than 1.0 and TOF fade ensued (partial block). When the fourth twitch in the TOF disappeared, the TOF ratio became 0 fade (moderate block and intense block).

In a phase I depolarizing blockade, the twitch height is diminished, but no fade is present.

The onset time was recorded (time from injection of neuromuscular blocking agent to maximal depression of the first twitch height (T1)) i. e., TOF ratio equal zero, the clinical duration of action of the muscle relaxants (time from injection of neuromuscular blocking agent to recovery of T1 to 25% of baseline), recovery time (time to recovery of T1 to 75% of baseline (T 75%) and recovery index (the difference between T 75% and T 25%).

Hemodynamic parameters including heart rate (HR) and mean arterial blood pressure (MAP) were monitored before induction of general anesthesia then at 1,3,5,10,15 and 20 minutes after muscle relaxant administration then every 10 minutes.

Maintenance of Anesthesia: .

Anesthesia was maintained with 1 % isoflurane with controlled ventilation by GE Datex-Ohmeda Aespire View Anesthesia Machine (Datex-Ohmeda Inc. Madison, WI 53707-7550 USA). TV 7-8 ml. kg^{-1}, respiratory rate 12-14 /minute and PEEP 5 cm H2O. Ventilation was controlled to maintain end tidal carbon dioxide at 35-40 mm Hg. Whenever the twitch response returned to 25% of control, increments of rocuronium by 0.1- 0.15 mg. kg^{-1} were administered in rocuronium group, increments of atracurium by 0.1-0.15 mg. kg^{-1}were administered in atracurium group and 0.2 mg. kg^{-1} atracurium in suxamethonium group when twitch height returns to normal. Anesthesia was supplemented with intravenous fentanyl2µg. kg^{-1}. After delivery, oxytocin infusion 20-30 units / l liter of crystalloid solution was given.

Reversal and recovery of the muscle relaxant: .

At completion of the operation after recovery data was measured, those patients who had received rocuronium or atracurium were given neostigmine 0.045 mg. kg^{-1} with atropine 0.01 mg. kg^{-1} before the extubation. The reversal administration was started after the appearance of all the four twitches. The time of administration of these drug was noted and reversal of paralysis shown by the ability of the patient to maintain a head lift for 5 seconds, patient can open her eyes widely and stick out her tongue and the fourth twitch was almost identical the first one. After extubation, all patients received morphine 0.1 mg. kg^{-1}in divided doses as analgesia.

Statistical Analysis and Statistical Package: .

Data were analyzed using SPSS 21.0 for Windows (SPSS, Chicago, IL, USA). Analysis of variance was used to compare the three groups for quantitative parametric data with post-hoc Tukey's test performed if there was a significant difference among the groups, a. Kruskal- wallis test was used for quantitative non parametric data. Chi square test was used for comparison of qualitative data. Continuous parametric data was presented as mean± SD, non-parametric data as median (IQR) and categorical data was presented as number of patients. P-values of <0.05 were considered significant and< 0.001 highly significant.

3. Results.

60 parturients were studied undergoing cesarean section, aged 18 to 37 years and physical status ASA I and II. According to the muscle relaxant used, patients were allocated randomly to receive one of the following drugs: G I was given 0.6 mg. kg-1 rocuronium (20 Patients); G II was given 0.5 mg. kg-1 atracurium (20 Patients); G III (control group) was given 1 mg. kg-1 succinylcholine just after propofol injection (20 Patients). The main findings of this study was that rocuronium (0.6 mg. kg^{-1}) and succinylcholine (1 mg. kg^{-1}) had excellent and good intubating conditions of 90% and 100% respectively, which was significantly higher than those for atracurium (75%). **(P-value <0.05)**.

Rocuronium had significantly shorter onset time than atracurium (64.45±16.38 sec. and 84.45±35.63 sec.) respectively and shorter clinical duration (35.95±5.64 min. and 40.75±5.89 min.) respectively **(P-value <0.05)**. Rocuronium had rapid onset of action approaching that of succinylcholine (rocuronium onset time was 64.45±16.38 sec. and succinylcholine onset time was 55.85±16.22 sec.).

Rocuronium had significantly shorter recovery time than atracurium (46.60±6.63 min. and 52.90±5.74 min.) respectively and had significantly lower number of patients with fade in TOF at 1 minute post its injection than atracurium (9 patients versus 17 patients) respectively. Number of patients with zero fade in TOF at 1 minute post injection of rocuronium was significantly higher than atracurium (11 patients versus 3 patients) **(P-value <0.05)**.

Rocuronium had significantly lower number of patients with no fade in TOF at 60 minutes post its injection than atracurium (no patients versus 5 patients) **(P-value <0.05)**.

Demographic data:

There was no significant difference among the three tested groups of the study as regards age, weight and ASA physical status classification (Table 1).

Table (1): Demographic characteristics of the patients in the three tested groups.

	Group I *(n=20)*	**Group II *(n=20)***	**Group III *(n=20)***	**p-value**
Age (years)	25.50±5.56	26.60±5.61	27.20±6.17	0.644
Weight (in kg)	59.50±8.15	63.85±6.52	63.85±7.75	0.120
ASA Grade I	16 (80.0%)	16 (80.0%)	18 (90.0%)	0.619
Grade II	4 (20.0%)	4 (20.0%)	2 (10.0%)	

Data are presented as mean ± SD, number of patients (%) p-value>0.05 is considered statistically non significant.

Hemodynamic parameters:

Heart rate:

The changes in heart rate for the tested groups are shown in Table 2 and Fig.10. There was no significant difference among the three groups for patients' baseline heart rates and after 15 minutes of intubation. Heart rate at 3-15 min was higher in group I than in group II and III **(P-value <0.05)**.

Table (2): Comparison between the three tested groups according to heart rate (Beat/min)

	Group I (n=20)	**Group II (n=20)**	**Group III (n=20)**	**p-value**
baseline	79.20±7.70	77.55±10.20	79.85±9.03	0.710
1min.	87.95±8.37	84.15±10.79	85.60±7.48	0.131
3min.	90.42±7.33	85.80±10.76†	86.25±8.48 †	0.039*
5min.	93.70±7.36	86.15±10.47†	88.55±8.92†	0.025*
10min.	96.20±7.52	87.90±10.39 †	89.47±9.00†	0.009*
15min	89.80±7.80	83.80±10.23 †	86.90±4.69†‡	0.026*
20min.	79.25±7.77	73.60±4.88	76.60±10.21	0.469
30min.	79.70±8.31	74.27±5.14	78.55±10.20	0.339
40min.	78.00±8.08	76.10±4.61	78.63±9.95	0.895
50min.	76.09±6.06	74.60±9.93	75.87±4.82	0.267
60min.	77.00±6.24	74.53±5.08	76.60±9.63	0.474

Data are presented as mean ± SD .

*p-value <0.05 is considered statistically significant between the 3groups.

† P-value <0.05 is considered statistically significant compared to group I.

‡ P-value <0.05 is considered statistically significant compared to group II.

Mean arterial pressure:

Changes in mean arterial pressure for the three tested groups are shown in Table 3 and Fig.11. There was no statistically significant difference between the three groups as regard with MAP at times 0,20,30,40,50,60 min. MAP at 1, 3,5 and 10 min. post intubation was higher in group I than in group II and group III **(P-value <0.05**).

Table (3): Comparison between the three tested groups according to MAP (mm Hg)

	Group I. (n=20)	**Group II. (n=20)**	**Group III. (n=20)**	**p-value**
baseline	89.25±8.05	85.65±10.11	89.95±9.02	0.284
1min.	100.05±8.36	92.25±10.70†	97.20±8.12†‡	0.019*
3min.	96.35±8.47	89.40±10.09†	94.05±7.67‡	0.027*
5min.	97.65±8.91	88.75±10.75†	94.75±7.70‡	0.014*
10min.	96.53±8.98	89.50±10.68†	90.30±7.92†	0.016*
15min.	93.90±8.20	86.05±10.26†	89.13±5.25†	0.027*
20min.	87.35±8.18	86.75±10.08	85.83±5.45	0.241
30min.	86.80±8.72	86.65±10.11	83.50±5.72	0.282
40min.	88.10±8.49	86.74±9.84	86.23±5.18	0.873
50min.	84.91±6.24	85.73±9.79	83.00±5.39	0.549
60min.	85.00±4.21	80.67±5.66	83.60±9.63	0.639

Data are presented as mean ± SD .
*p-value <0.05 is considered statistically significant between the 3groups.
† P-value <0.05 is considered statistically significant compared to group I.
‡ P-value <0.05 is considered statistically significant compared to group II.

The intubation condition during laryngoscopy after rocuronium bromide and atracurium in comparison with succinylcholine:.

The intubation conditions for the tested drugs are shown in Table 4 and Fig.12. The intubating conditions at 60 seconds in rocuronium group were excellent in 60% and good in 30 %, two patients who received rocuronium, the trachea could not be intubated at 60 seconds due to closed vocal cords and considered as poor intubating condition but intubation was possible 60 seconds later. The intubation conditions at 60 seconds in atracurium group were excellent in 40% and good in 35 %, 5 patients who received atracurium, the trachea could not be intubated at 60 seconds due to closed vocal cords and considered as poor intubating condition but intubation was possible 60 seconds later. The intubation conditions at 60 seconds in succinylcholine group were excellent in 75% and good in 25 %. There was significant difference between the three groups according to intubation condition. The number of cases with excellent and good intubation condition for the three tested groups was significantly higher in group III than in group I and group II **(P-value <0.05**).

Table (4): Comparison between the three groups according to intubation condition.

Intubation condition	**Group I . *(n=20)***	**Group II . *(n=20)***	**Group III . *(n=20)***	**p-value**
Excellent	12 (60.0%)	8 (40.0%)	15 (75.0%)†‡	0.036*
Good	6 (30.0%)	7 (35.0%)	5 (25.0%)‡	
Poor	2 (10.0%)	5 (25.0%)	0 (0.0%)	

Data are presented as mean ± SD .
*p-value <0.05 is considered statistically significant between the 3 groups.
† P-value <0.05 is considered statistically significant compared to group I.
‡ P-value <0.05 is considered statistically significant compared to group II.

The onset time and the clinical duration of the three groups:.

The onset time and the clinical duration of the three tested groups are shown in Table 5 and Fig.13, 14. and indicate that the onset time of group II was 84.45±35.63 sec., significantly longer than the onset time of 64.45±16.38 sec. for group I and the onset time of 55.85±16.22 sec. for group III. The clinical duration of atracurium was 40.75±5.89 min., significantly longer than clinical duration of 35.95±5.64 min. for group I and the clinical duration of 7.35±1.46 min. for group III.

Table (5): Comparison between the three tested groups according to the onset time and the clinical duration.

Onset time and the clinical duration	Group I *(n=20)*	Group II *(n=20)*	Group III *(n=20)*	p-value
Onset time (sec.)	64.45±16.38	84.45±35.63†	55.85±16.22‡	0.002*
Clinical duration (min.)	35.95±5.64	40.75±5.89†	7.35±1.46†‡	<0.001**

Data are presented as mean ± SD *p-value <0.05 is considered statistically significant between the 3groups.
***p-value <0.001 HS*† P-value <0.05 is considered statistically significant compared to group I.
‡ P-value <0.05 is considered statistically significant compared to group II.

The recovery time and the recovery index.

The recovery time and the recovery index of the three tested groups are shown in Table 6 and Fig.15. and indicate that the recovery time of group II was 52.90±5.74 min., significantly longer than recovery time of 46.60±6.63 min. for group I and the recovery time of 10.10±1.33 min. for group III **(P-value <0.05)**.

The recovery index of group II was 12.15±1.60 min., significantly longer than recovery index of 10.65±2.21 min. for group I and the recovery index of 2.80±0.77 min for group III **(P-value <0.05)** (**Table 6**).

Table (6): Comparison between the three tested groups according to the recovery time and recovery index.

Recovery time and index	Group I *(n=20)*	Group II *(n=20)*	Group III *(n=20)*	p-value
Recovery time (min.)	46.60±6.63	52.90±5.74†	10.10±1.33†‡	<0.001**
Recovery index (min.)	10.65±2.21	12.15±1.60	2.80±0.77†‡	<0.001**

Data are presented as mean ± SD*p-value <0.05 is considered statistically significant between the 3groups .
**p-value <0.001 HS † P-value <0.05 is considered statistically significant compared to group I.
‡ P-value <0.05 is considered statistically significant compared to group II.

Subjective TOF ratio.

Subjective TOF ratio of the three tested groups are shown in Table 7 There was no significant difference among the three groups for patients' baseline subjective TOF ratio. There was statistically significant difference between the three groups according to subjective TOF ratio until reverse of NDMRs in group I and group II or until recovery of T1 to 25% of baseline in group III **(P-value <0.05)**. There was no fade in TOF in group III from before its onset to its recovery. Number of patients with fade in TOF at 1 minute post injection of NDMR was higher in group II (17 patients) than group I (9 patients). 3 patients in group II had fade in TOF at 2 minutes post injection with no patients in group I. 1 patient in group II had fade in TOF at 3 minutes post injection with no patients in group I.

Number of patients with zero fade in TOF at 1 minute post injection of NDMR was higher in group I (11 patients) than group II (3 patients). Number of patients with zero fade in TOF at 2 minutes post injection of NDMR was higher in group I (20 patients) than group II (17 patients). Number of patients with zero fade in TOF at 3 minutes post injection of NDMR was higher in group I (20 patients) than group II (19 patients).

Number of patients with no fade in TOF at 45 minute post injection of NDMR was higher in group II (17patients) than group I (10 patients). Number of patients with no fade in TOF at 50 minutes post injection of NDMR was higher in group II (13 patients) than group I (9 patients). Number of patients with no fade in TOF at 55 minutes post injection of NDMR was higher in group II (9 patients) than group I (3 patients). 5 patients in group II had fade in TOF at 60 minutes post injection with no patients in group I.

4. Discussion.

The main findings of this study was rocuronium gave good and excellent intubating conditions significantly higher than atracurium and comparable to intubation following succinylcholine.

Rocuronium had significantly shorter onset time and clinical duration than atracurium and had rapid onset of action approaching that of succinylcholine. It had significantly shorter recovery time than atracurium and had significantly lower number of patients with fade in TOF at 1 minute post its injection than atracurium. Number of patients with zero fade in TOF at 1 minute post injection of rocuronium was significantly higher than atracurium. Rocuronium had significantly lower number of patients with no fade in TOF at 60 minutes post injection of NDMR than atracurium.

This study was conducted on 60 parturients delivered by elective cesarean section. Aged 18 to 37 years and physical status ASA I and II. They were divided into 3 groups: group I was given 0.6 mg. kg-1 rocuronium (n = 20), group II was given 0.5 mg. kg-1 atracurium (n = 20) and group III was given 1 mg. kg-1 succinylcholine (n = 20).

Table (7): Comparison between the three tested groups according to the subjective TOF ratio at various time intervals.

TOF	Group I *(n=20)*	Group II *(n=20)*	Group III *(n=20)*	p-value
Basal				
No Fade	20 (100 %)	20 (100%)	20 (100 %)	1.000
1 min.				
Fade	9 (45 %)	17 (85 %)	0 (0 %)	<0.001*‡
No Fade	0 (0 %)	0 (0 %)	20 (100%)	
Zero Fade	11 (55 %).	3 (15%)	0 (0 %)	
		0.02†		
2 min.				
Fade	0 (0 %)	3 (15 %)	0 (0 %)	<0.001*‡
No Fade	0 (0 %)	0 (0 %)	20(100%)	
Zero Fade	20 (100 %)	17 (85 %)	0 (0.%)	
3 min.				
Fade	0 (0 %)	1 (5 %)	0 (0 %)	<0.001*‡
No Fade	0 (0 %)	0 (0 %)	20 (100 %)	
Zero Fade	20 (100 %)	19 (95 %)	0 (0 %)	
5 min.				
No Fade	0 (0 %)	0 (0 %)	20 (100 %)	<0.001*‡
Zero Fade	20 (100 %)	20 (100 %)	0 (0 %)	
10 min.				
No Fade	0 (0 %)	0 (0 %)	13/13 (100%)	<0.001*‡
Zero Fade	20 (100 %)	20 (100 %)	0 (0 %)	
15 min.				
Zero Fade	20 (100.0%)	20 (100.0%)	0 (0.0%)	<0.001*‡
20 min.				
Fade	11 (55 %)	8 (40 %)	0 (0 %)	<0.001*‡
Zero Fade	9 (45 %)	12 (60 %)	0 (0 %)	
25 min.				
Fade	20 (100 %)	18 (90 %)	0 (0 %)	<0.001*‡
Zero Fade	0 (0 %)	2 (10 %)	0 (0 %)	
30 min.				
Fade	10 (50 %)	13 (65 %)	0 (0 %)	<0.001*‡
No Fade	10 (50 %)	7 (35 %)	0 (0 %)	
35 min.				
Fade	9 (45.0%)	13/19 (68.4%)	0 (0 %)	<0.001*‡
No Fade	11 (55.0%)	6/19 (31.6%)	0 (0 %)	
40 min.				
Fade	0 (0 %)	2/19 (10 %)	0 (0 %)	<0.001*‡
No Fade	19/19(100%)	17/19 (90%)	0 (0 %)	
45 min.				
No Fade	10/10(100%)	17/17 (100%)	0 (0 %)	<0.001*‡
50 min.				
No Fade	9/9(100%)	13/13(100%)	0 (0 %)	<0.001*‡
55 min.				
No Fade	3/3 (100%)	9/9(100%)	0 (0 %)	<0.001*‡
60 min. No Fade	0/0 (0%)	5/5(100%)	0 (0.0%)	0.004*‡
		0.032†		

Data are presented as number of patients (%).

*p-value <0.05 is considered statistically significant between the 3groups.

† P-value <0.05 is considered statistically significant compared to group I.

‡ P-value <0.05 is considered statistically significant between group III & groups I & II.

Neuromuscular block was assessed by stimulation of ulnar nerve at wrist at adductor pollicis muscle using a "Micro stim" peripheral nerve stimulator. Subjective (visual /tactile) TOF ratio was recorded at 0, 1, 2 and 3 minutes from injection of the muscle relaxant and then every 5 minutes until reversal of muscle relaxant.

The choice of anesthesia for cesarean section relies on the indication for the operation, the degree of urgency of required intervention, the maternal and/or fetal status, the patients' desires and skill of the anesthesiologist. The anesthesiologist should choose the anesthesia method that he believes to be the safest and the most comfortable for the parturient and the least depressant to the newborn.

General anesthesia is the quickest anesthesia method in an emergency and is considered the method of choice in some conditions. It may be indicated when the parturient refuses the regional anesthesia, failed regional attempts or when regional is contraindicated such as in coagulopathy or spinal abnormalities.

Failed end tracheal intubation and aspiration of gastric contents are considered the two major causes of maternal mortality that associated with GA. Women undergone general anesthesia for caesarean section; need a rapid sequence induction to protect against pulmonary aspiration. Succinylcholine is the most commonly used muscle relaxant as its fast onset and short duration but it has many serious complications.

Rocuronium a new muscle relaxant with a brief onset of action, but devoid of the succinylcholine adverse effects may be a suitable alternative to it and to test this hypothesis. This study compared the intubating and recovery characteristic of succinylcholine, rocuronium and atracurium for caesarean section.

The results of the comparison between intubating & recovery characteristics of succinylcholine (Group III), rocuronium (Group I) and atracurium (Group II) in parturients undergoing cesarean sections have many findings.

All the groups in our study were comparable with respect to age, weight and ASA physical status classification thus demographically similar. There was no statistically significant difference between the three groups.

In this study, the hemodynamic parameters measured at baseline were comparable in all the three groups. The present study showed that among the three groups, there was a statistically significant increase in heart rate and MAP in rocuronium group after 3 minute post laryngoscopy and intubation when compared to other two groups. This is consistent with the study of Neeti M and colleagues, who attributed it to the weak vagolytic property of rocuronium ***(Kalpana, K et al. 2014).***

This study showed that no clinically significant cardiovascular events (i. e. changes in arterial pressure or heart rate 30% above or below baseline values) occurring within 10 min of administration of the studied drugs. This is consistent with the study of Atia Ahmed et al who showed that there were no evidences of any substantial clinical cardiovascular changes in rocuronium group and atracurium group, and this is consistent with other previously reported studies observed no dose-related changes in heart rate and blood pressure after rocuronium ***(Atia Ahmed et al., 2017).***

The rise in pulse rate and MAP during laryngoscopy and intubation is either due to the stimulation of epipharynx and laryngopharynx or can be due to the light plane of anesthesia. It is predictable that endotracheal intubation will generate a pressor response though it can be subdued with the help of incorporating other drugs, for example, β-blockers, opioids, lignocaine, and Ca channel blockers, etc ***(Rout et al., 2017).***

In this study, we did not use any drug such as lidocaine and esmolol to attenuate the pressor response before laryngoscopy and intubation and by the end of 15 min, the pressor response was over and the values returned to near their baseline level.

Schramm WM et al concluded in their study that patients in the rocuronium group showed significant increase in heart rate that may be due to a vagal blocking effect ***(Dwivedi, Manisha Bhatt et al., 2015).***

Rout et al showed that the cardiovascular effects of muscle relaxants may be produced by muscarinic receptor block, ganglion block, increased noradrenaline release or blockage of its reuptake, and histamine liberation ***(Rout et al., 2017).***

In this study, the heart rate and the mean arterial blood pressure increased in atracurium group significantly at 1 min after intubation, though, HR and MAPreturned near the base line at 5 min and this is consistent with study of Mohamed, Ayman A et al who showed in their study that the heart rate and the mean arterial blood pressure increased in atracurium group significantly at 1 min after intubation due to the stress response, however, HR and MABP returned near the base line at 5 min ***(Mohamed, Ayman A. et al., 2012) .***

In this study, it was noted that the least hemodynamic change was in atracurium group when we compared it to other two groups and atracurium has clinical acceptable cardiovascular stability. This is consistent with Dhumane Pradeep et al who showed that atracurium has clinical acceptable cardiovascular stability ***(Dhumane Pradeep et al., 2016).***

In this study, the number of cases with acceptable intubation condition for the three tested groups was significantly higher insuccinylcholine group when it was compared to other two groups.

This study showed that rocuronium bromide is a neuromuscular blocking drug with good and excellent intubation condition approaching that of succinylcholine. Good and excellent intubation condition in 90% of patients of rocuronium group versus good and excellent intubation condition in 100%of patients succinylcholine group butte good and excellent intubation condition after atracurium administration was 75%. This is consistent with study of Lam, Arthur et al who concluded in their study that rocuronium bromide at a dose of 0.6 mg/kg, when used with propofol and fentanyl for induction, provides intubating conditions similar to succinylcholine 1.0 mg/kg at 1 minute ***(Lam, Arthur et al., 2000).***

Magorian et al observed that there was no difference in intubating conditions between the succinylcholine group and the rocuronium group ***(Lam, Arthur et al., 2000).***

Misra, M. N et al also concluded in their study that rocuronium produces intubating conditions which are satisfactory in comparison to succinylcholine ***(Misra, M. N et al., 2005).***

Venkateswaran et al showed that rocuronium in dose of 0.6 mg/kg gives clinically acceptable intubating conditions at 60 or 90 s, comparable to succinylcholine 1 mg/kg ***(Venkateswaran et al., 2012)***.

Dwivedi, Manisha Bhatt et al concluded that rocuronium may be considered a suitable alternative for succinylcholine especially in patients who are at risk of adverse effects of succinylcholine (**Dwivedi, Manisha Bhatt et al., 2015**).

Study by Tran D. T. T et al, showed that succinylcholine creates better intubation circumstances than rocuronium. However, if an alternative agent is required, rocuronium 1 mg. kg−1 can be used to create acceptable intubation conditions ***(Tran, D. T. T et al., 2017).***

In this study, the onset time and the clinical duration of atracurium were significantly longer when compared to other two groups and the onset time and the clinical duration are both significantly shorter with succinylcholine. This is consistent with the study of Xue, Fu-Shan et al who showed in their study that as compared to atracurium, the duration of action of rocuronium was shorter ***(Xue, Fu-Shan et al., 2007).***

Our study showed that the onset time of atracurium besylate was longer than the onset time of rocuronium bromide. 84.45±35.63 sec versus 64.45±16.38 sec and the clinical duration of atracurium besylate was longer than clinical duration ofrocuroniumbromide.40.75±5.89 min. versus 35.95±5.64 min. This is consistent with study of Atia Ahmed et al who showed in their study that the main onset of action of atracurium was found to be 68.75±11.2sec, in comparison to rocuronium onset of action 64.40±8.6sec. Further, the main duration of action of rocuronium was 33.57±3 min, while in atracurium, the duration was 35.45±5 min ***(Atia Ahmed et al., 2017).***

Our study showed that rocuronium bromide is a neuromuscular blocking drug with rapid onset of action after a dose of 0.6 mg/kg approaching than of succinylcholine. The onset time was 64.45±16.38sec in rocuronium versus 55.85±16.22 sec in succinylcholine but the onset time of atracurium was 84.45±35.63 sec. This is consistent with the study of Lam, Arthur et al who showed that, the onset time and clinical duration (time to 25% T1 recovery) are both significantly shorter with succinylcholine and compared to other non-depolarizing muscle relaxants, rocuronium has the quickest onset time and is considered as an alternative to succinylcholine without the adverse side effects associated with the latter ***(Lam, Arthur et al., 2000).***

The rapid onset of rocuronium correlate with previous study done by Levy et al Also Lowry et al who recorded the onset time of about one minute after rocuronium 0.6 mg/kg. This is parallel with previous study done by Puhringer et al who reported an onset time of about 1 min. In contrast Zhou et al demonstrated less rapid onset after 0.6 mg/kg rocuronium (141±65sec) ***(Omera, Magdy et al.,2005).***

This study showed that the onset time of rocuronium was 64.45±16.38sec and the onset time of succinylcholine was 55.85±16.22 sec. This is consistent with the study of Kumar et al who showed in their study that the mean onset time in succinylcholine group patients was 64.5 seconds with a SD of 10.84 and rocuronium group patients was 71. 5 seconds with an SD of 17.56***(Kumar et al., 2016).***

This study is consistent with the study of Patel, Kiran B et al who showed that Until now, suxamethonium remains the muscle relaxant of choice for rapid sequence induction in patient with full stomach because it offers a brief onset time reliably optimal intubating condition and a brief duration of action ***(Patel, Kiran B et al., 2014).***

Abu-Halaweh et al concluded in their study that rocuronium bromide 1 mg/kg can be safely used for rapid sequence induction in cesarean section and the intubating conditions are similar to those of suxamethonium **(Abu-*Halaweh et al.,2007).***

Rocuronium and atracurium are considered neuromuscular blockers of intermediate duration and our study has confirmed such classification. This is consistent with the study of Módolo, Norma Sueli

Pinheiro et al who showed in their study that atracurium and rocuronium are the neuromuscular blockers of intermediate duration and their study has confirmed such classification (**Módolo, Norma Sueli Pinheiro et al.,2002)**. Our study is consistent with the study of Xue, Fu-Shan et al who showed in their study that atracurium and rocuronium are low-potency nondepolarizing relaxants with intermediate duration ***(Xue, Fu-Shan et al.,2007)***.

In this study, the recovery time of atracurium was 52.90±5.74 min. significantly longer than recovery time of 46.60±6.63 min. for rocuroniumbromide and the recovery time of10.10±1.33 min. for succinylcholine. The recovery index of atracurium besylate was 12.15±1.60 min., significantly longer than recovery index of 10.65±2.21min. for R. Band the recovery index of2.80±0.77 min. for S. Ch. This is consistent with the study of Atia Ahmed et al who concluded in their study that the onset of action, clinical duration, and recovery index of rocuronium was much better compared to atracurium ***(Atia Ahmed et al., 2017).***

The results of this study are consistent with what Barash, Paul G. showed that the recovery index of atracurium is 10-15 min., the recovery index of rocuroniumbromide is 8-12 min. and the recovery index of succinylcholine is 2-4 min. ***(Barash, Paul G et al., 2013).***

This study is consistent with the study of Kaur, Harpreet et al who showed in their study that the recovery time of atracurium besylate was 51.75±9.46 min. and the recovery index of atracurium besylate was 14.63±1.84 min. ***(Kaur, Harpreet et al., 2018).***

In this study, there was no significant difference among the three groups for patients' baseline subjective TOF ratio. There was statistically significant difference between the three groups according to subjective TOF ratio until reverse of non-depolarized MR in rocuronium and atracurium group or until recovery of T1 to 25% of baseline in suxamethonium group. The major limitation to this study was that the perception of TOF fade was subjective. Such subjective evaluation is the most commonly used method of evaluating the depth of neuromuscular block and adequacy of reversal ***(Brull, Sorin J et al., 2017).***

It is known that when neuromuscular monitoring is used, visual or tactile evaluation of the degree of neuromuscular block is unreliable. Even experienced anesthetists are can not detect fade when the TOF ratio is > 0.4***(Mc Grath et al., 2006)***. The previous studies have shown that it is difficult to detect tactile fade of TOF at a TOF ratio > 0.4 ***(Song, I. A. et al., 2015).*** Objective measurement (a train-of-four ratio greater than 0.90) is the only method to determine appropriate timing of tracheal extubation and ensure normal muscle function and patient safety ***(Brull, Sorin J et al., 2017)***. But when a quantitative PNS monitor is not available we can use a qualitative PNS monitor as Thilen SRv et al showed in their study that when a quantitative PNS monitor is not available and we use a qualitative PNS monitor, it is critical to maximize the chances of a successful reversal. This is most reliably accomplished by confirming an adequate level of spontaneous recovery prior to administration of neostigmine. This can be considered the most critical aspect of management when aiming to prevent residual paralysis while using a qualitative PNS monitor and neostigmine ***(Thilen SR et al., 2016).*** Though evidence strongly suggests that quantitative monitors must be used intraoperatively whenever NMBAs are administered, these devices are not widely available ***(Brull, Sorin J et al., 2017).***

This study showed that there was no fade in TOF in suxamethonium group from before its onset to its recovery. This is consistent with the study of Mc Grath et al who showed in their study that the TOF pattern is less useful in monitoring depolarizing neuromuscular block. During onset of depolarizing block, each of the four twitches is decreased equally in size, that is, there is no fade. This is also observed during recovery (Mc Grath et al.,2006). Miller, R. D et al showed that during a partial depolarizing block, no fade occurs in the TOF response; ideally, the TOF ratio is about 1.0 (Miller, R. D et al.,2010). Morgan GE et al showed that a phase I depolarization block does not show fade during tetanus or train of four; neither does it demonstrate post tetanic potentiation. If enough depolarizer is administered, however, the quality of the block changes to resemble a nondepolarizing block (phase II block) ***(Morgan GE et al., 2013).***

The present study showed that number of patients with fade in TOF at 1 minute post injection of non depolarizing MR was higher inatracurium group (17 patients) than rocuronium group (9 patients). 3 patients in atracurium had fade in TOF at 2 minutes post injection with no patients in rocuronium group. 1 patient in atracurium had fade in TOF at 3 minutes post injection with no patients in rocuronium group. This denote that atracurium the onset time of atracurium besylate longer than the onset time of rocuronium bromide as fade in TOF occur in partial nondepolarizing block. Miller, R. D et al showed that during a partial nondepolarizing block, the ratio decreases (fades) and is inversely proportional to the degree of blockade ***(Miller, R. D et al., 2010).***

The present study showed that number of patients with zero fade in TOF at 1 minute post injection of non depolarizing MR was higher inrocuronium group (11 patients) than atracurium group (3 patients). Number of patients with zero fade

in TOF at 2 minutes post injection of non depolarizing MR was higher inrocuronium group (20 patients) than atracurium group (17 patients). Number of patients with zero fade in TOF at 3 minutes post injection of non-depolarizing MR was higher inrocuronium group (20 patients) than atracurium group (19 patients). This denote that the onset time of rocuronium bromide shorter than the onset time of atracurium besylate as zero fade in TOF occur in deep nondepolarizing block. As the nondepolarizing block becomes more intense, T4 disappears followed by T3, T2, and finally T1 ***(Mc Grath et al., 2006).*** Thilen SR et al showed that if the block is too deep for TOF monitoring, i. e., there are no twitches in the TOF response, then post-tetanic count (PTC) must be used for monitoring ***(Thilen SR et al., 2016).***

This study showed that number of patients with no fade in TOF at 45 minute post injection of non depolarizing MR was higher inatracurium group (17 patients) than rocuronium group (10 patients). Number of patients with no fade in TOF at 50 minutes post injection of non depolarizing MR was higher inatracurium group (13 patients) than rocuronium group (9 patients). Number of patients with no fade in TOF at 55 minutes post injection of non depolarizing MR was higher inatracurium group (9 patients) than rocuronium group (3 patients). 5 patients in atracurium had fade in TOF at 60 minutes post injection with no patients in rocuronium group. This denote that the clinical duration of atracurium is longer than the clinical duration of rocuronium bromide. Morgan GE et al showed that adequate clinical recovery correlates well with the absence of fade ***(Morgan GE et al., 2013)***. Naguib, M. et al showed that after the administration of a non-depolarising neuromuscular blocking drug, a progressive reduction in the amplitude of four twitches is observed with the fourth twitch being most affected. As the block progresses, the first response to disappear is the fourth twitch, followed by the third, second and finally the first twitch. This order of reappearance is reversed during the recovery phase (T1 is the first twitch to recover) ***(Naguib, M. et al., 2017).***

To our knowledge, this is the first study to compare between intubating & recovery characteristics of succinylcholine, rocuronium and atracurium in parturients undergoing cesarean sections.

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Conclusion and Recommendations .

As regarding the present study, rocuronium bromide 0.6mg/kg can be safely used for rapid sequence induction in part urients under going cesarean sections and the intubating conditions are similar to those of suxamethonium.

Recommendations.

1. Further studies on large number of patients are needed for better judgment on using rocuronium bromide as a good alternative to suxamethonium for tracheal intubation in cesarean sections.
2. Use rocuronium bromide alternative to suxamethonium for tracheal intubation in cesarean sections.
3. Any hospital should be provided by rocuronium bromide. It should be used when suxamethonium is contraindicated or when its use is hazardous.
4. Further studies on large number of patients are needed for finding the ideal neuromuscular blocking agent which has rapid onset time and offers good to excellent intubation conditions with no side effects .

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