

## Efficacy And Safety Of Sugammadex In Reversing Nmb (Rocuronium) In Adults

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**Abstract: Background And Objective:** Sugammadex reverses neuromuscular blockade induced by aminosteroid agents by encapsulating these agents. This study designed to assess safety and efficacy of sugammadex in reversing rocuronium-induced neuromuscular blockade. **Patients And Methods:** One hundred ASA 1-2 patients aged 20 - 40 years scheduled for short elective surgery were allocated and divided into 5 equal groups (A, B, C, D and E). Rocuronium administered in a dosage of 0.6 mg / kg for patients of groups A, B, C and D, and administered in a dose of 1.2 mg/kg for the 5<sup>th</sup> group (E). After surgery, neostigmine 50 mic/kg with atropine 0.015 mg/kg was administered on train-of-four (TOF) 0.2 for group A patients while sugammadex was administered in a dosage of 3 mg / kg on (TOF) 0.2 for group B patients. patients of group C and D received sugammadex on TOF 0.0 with PTC stimulation recorded in a dose of 3 mg/kg and 6 mg/kg respectively. While the patients of the group E received sugammadex in a dose of 1.2 mg/kg on TOF 0.0 with PTC stimulation recorded. Times until recovery of T4/T1 ratios 0.9 were recorded. **Results:** Time between sugammadex administration until recovery of a TOF ratio of 0.9 was shorter for patients of group B than group A (mean [SD], 78. [16.75] seconds and 213.1 [48.8] seconds, respectively), which is highly significant. While patients of group C and D times were (126.8 [26.8] seconds and 84.78 [17.05] seconds respectively), also highly significant. patients of group E, time was 70.5[8.56]. No signs of recurarization, residual paralysis or associated serious adverse effects were observed for all patients.

**Conclusion:** Sugammadex effectively and safely reverses a rocuronium-induced neuromuscular blockade significantly faster than neostigmine and in a reverse pattern (increasing the dose decreasing the time).

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**Keywords:** Sugammadex; neostigmine; reoccurrence of neuromuscular block; reversal agent, residual paralysis, rocuronium, selective relaxant binding agent

### 1. Introduction

Since the introduction of curare to anesthesia in the 1940s neuromuscular blockade has played a pivotal role in facilitating anesthetic, surgical, and critical care practice. (1). In 1988, rocuronium was found to achieve intubation conditions almost as rapidly as suxamethonium if administered in a sufficiently large dose (1.2 mg/kg). It has therefore become popular as an alternative neuromuscular blocker for RSI (2). However, the intermediate duration of action of the intubating dose of rocuronium is an obvious disadvantage for short surgical procedures and can create serious problems should there be unexpected difficulty in securing the airway (3).

Reversal of neuromuscular blockade is important for the acceleration of patient recovery and prevention of postoperative residual neuromuscular blockade (4). Currently, the reversal of neuromuscular blockade is achieved by the administration of acetylcholinesterase inhibitors (5). Acetylcholinesterase inhibitors have some problems with their use. The duration of action of all currently available nondepolarizing muscle

relaxants is too long for early or “escape” reversal after a short case or an unexpected cannot intubate, cannot-ventilate scenario using neostigmine (3). The inability of cholinesterase inhibitors to reverse a profound nondepolarizing blockade may be one important reason for the persistence of succinylcholine in current anesthetic practice for rapid sequence induction and ultra short procedures (6).

Acetyl cholinesterase inhibitors have unwanted effects associated with stimulation of the muscarinic receptors resulting in bradycardia, arrhythmias, increased secretions and contraction of smooth muscle, though these can be counteracted by administration of muscarinic antagonists (atropine or glycopyrrolate) (7). Muscarinic antagonists also have side effects as blurred vision, dry mouth and tachycardia (1).

As a consequence, research continued for the ideal reversal agent. In 2001, a modified  $\gamma$ -cyclodextrin, sugammadex (Org 25969) was discovered by Bom et al (8). This modified  $\gamma$ -cyclodextrin encapsulates rocuronium in a 1:1 ratio decreasing its plasma concentration to zero (9).

Sugammadex quickly inactivated rocuronium by encapsulation, reversing its neuromuscular blocking effects. In 2005, the first exposure of sugammadex to human volunteers was reported to be safe and effective (10).

## 2. Patients and Methods

The research protocol was approved by scientific committee of anesthesia department and then patients enrollment started after the study protocol approved by the local Ethics and Research Committee of the Departments of Anaesthesia, ICU and Pain Management Benha faculty of medicine, Benha University.

Patients eligible for inclusion were aged 20 – 40 years with American Society of Anesthesiologists physical status of I or II and scheduled to undergo short elective surgery of less than 15 minutes duration under general anesthesia and rocuronium bromide as muscle relaxation for intubation, these surgery include piles, anal fissure, anal fistulae lipoma excision, dilatation and or curettage of uterine contents.

Exclusion criteria included a known or a suspected neuromuscular disorders, hepatic or renal dysfunction, anatomical malformations expected to result in a difficult intubation (Mallampati score 3 and 4) deviation from average body mass index (BMI)  $\geq 25\%$ , pregnancy, administration of any type of medication known to interfere with NMBAs (anticonvulsants, aminoglycosides, and magnesium-containing medications), known or suspected personal or family history of malignant hyperthermia, known or suspected allergy to narcotics, muscle relaxants, or any other medication used during general anesthesia. In addition, women of childbearing age not using an acceptable method of birth control and those who were breast feeding were not eligible for the study.

One hundred adult patients were included in this study and after getting written informed consent from all of them, they were divided randomly into 5 equal groups of 20 patients each:

1- Group A:- where neuromuscular blocker is rocuronium in a dose of 0.6 mg/kg and the reversal drug used was neostigmine in a dose of 0.05 mg/kg plus atropine in a dose of 0.015 mg/kg and reversal time start after end of surgery and as soon as TOF 0.2 was achieved.

2- Group B:- where neuromuscular blocker is rocuronium in a dose of 0.6 mg/kg and the reversal drug used was sugammadex in a dose of 3 mg/kg and reversal time start after end of surgery and as soon as TOF 0.2 was achieved.

3- Group C: where neuromuscular blocker is rocuronium in a dose of 0.6 mg/kg and the reversal drug used was sugammadex in a dose of 3 mg/kg and

the reversal time start immediately after end of surgery and TOF was still 0.0 and PTC values recorded.

4- Group D: where neuromuscular blocker is rocuronium in a dose of 0.6 mg/kg and the reversal drug used was sugammadex in a dose of 6 mg/kg and reversal time start immediately after end of surgery and TOF was still 0.0 and PTC values recorded.

5- Group E: - where neuromuscular blocker is rocuronium in a dose of 1.2 mg/kg and the reversal drug used was sugammadex in a dose of 12 mg/kg and reversal time start immediately after end of surgery and TOF was still 0.0 and PTC values recorded.

On arrival in the operating room, routine monitors were applied for recording heart rate (HR), mean arterial blood pressure (MAP), and oxygen saturation values. The TOF-Watch SX (Organon Ltd., Dublin, Ireland) is turned on and the connection with laptop via its specific interphase is carried out and then registration of patient personal data and the vital signs measurements were recorded too. Surface electrodes (Red Dot R3M Health Care, Neuss, Germany) were placed on the cleaned skin over the ulnar nerve of the wrist one inch apart with the black positive electrode distally and the white negative electrode proximally and the acceleration transducer of a TOF Watch SX (Organon) was fixed to the volar side of the distal phalanx of the respective thumb on a small elastic hand adapter (TOF Watch SX Hand adapter, Organon). The current was manually set at 40 mA and TOF stimulation at the predetermined supramaximal threshold (at a pulse width of 0.2 ms and 2 Hz frequency). The monitored arm was immobilized on an arm board. A temperature sensor, fixed at the palm of the hand ensured that the skin temperature of the monitored arm was maintained at greater than 35°C.

Data were registered and transferred in real-time via an interface (TOF-Watch®-SX Monitor, version 2.5 INT Organon) to a laptop computer in the operating room.

No premedication was given to any patient before induction. After 3 min of pre oxygenation, general anesthesia was induced by fentanyl 1 $\mu$ g/kg and propofol sleeping dose, as soon as verbal communication was lost assisted ventilation with 100% oxygen by facemask was started. Then the TOF-Watch® SX was switched to a single train-of-four stimulation and the reading was recorded and considered as control. Immediately after administration of the single bolus dose of rocuronium (Esmeron®; NV Organon, Oss, The Netherlands) of 0.6 mg/kg in groups A, B, C and D; while in groups E rocuronium dose was 1.2 mg/kg, the TOF stimulation was switched to the repetitive train-of-four stimulation every 15 second until the reading becomes 0.0, a direct laryngoscopy was initiated and followed by tracheal intubation.

Anesthesia was maintained with isoflurane 1%, routine monitoring included electrocardiography, pulse oximetry and noninvasive blood pressure monitoring. Neuromuscular transmission by the acceleromyographic response of the adductor pollicis muscle to repetitive train-of-four stimulation of the ulnar nerve times and readings were also recorded.

At the end of surgery the acceleromyography was set for TOF stimulation every 15 seconds permitting continuous measurement and as soon as the TOF achieves 0.2, reversal drug was immediately injected, the reversal drug was neostigmine in a dose of 0.05 mg/kg plus atropine in a dose of 0.015 mg/kg in group A, while in group B the reversal drug was sugammadex 3 mg/kg and neuromuscular monitoring was continued until TOF ratio of 0.9 has been achieved in all patients of the two groups. While in the other three groups the acceleromyography was set for TOF stimulation every 15 second permitting continuous measurement of the acceleration of the thumb and at the end of surgery while the TOF is still 0.0 injection of sugammadex in a dose of 3 mg/kg, 6 mg/kg and 12 mg/kg for patients in group C, D, and E respectively and the monitoring was continued until a TOF ratio of 0.9 has been achieved in all patients of the three groups.

Noninvasive mean arterial pressure (MAP) and heart rate (HR) measurements were obtained immediately before and after administration of the reversal drugs and subsequently at 2, 5, 10, 20 and 30 minutes. In addition, after recovery of the T4/T1 ratio to 0.9, oxygen saturation, respiratory frequency, and clinical evidence of residual curarization were monitored for 30 minutes. Side effects and/or clinical evidence of RP or reoccurrence of neuromuscular blockade for 60 minutes to be recorded.

Primary endpoint was defined as the time from injection of reversal drug either sugammadex or neostigmine with atropine to the time of achievement of TOF ratio of 0.9. Secondary endpoint was recording any clinical sign of muscle weakness, clinical evidence of residual curarization as well as any side effects immediately after injection of reversal drug and for 30 minutes after injection of the reversal drug.

#### **Sample size and power of the study**

Our sample size was calculated to achieve a power of  $> 0.95$  at an  $\alpha$  error of 0.05 to detect a significant difference between sugammadex using different doses and neostigmine antagonism of rocuronium-induced neuromuscular blockade, 16 patients were required. To allow for dropouts, we randomized 20 patients.

#### **Statistical Analysis:**

Data were described in terms of mean, (SD) and range or frequencies and percentages, as appropriate. Comparison of continuous variables was done using one way analysis of variance (ANOVA) test with post-hoc multiple 5-group comparisons. Within group comparison of numerical variables between baseline and postoperative values was done using paired *t* test. Within group comparison over many time points was done using paired *t* test as post-hoc multiple comparison tests with Bonferroni adjusted *p* values. For comparing categorical data, Chi square ( $\chi^2$ ) test was performed. Fisher Exact test was used instead when the expected frequency is less than 5. *P* values  $> 0.05$  denotes statistically non significant however, *p* values less than 0.05 ( $*P < 0.05$ ) was considered statistically significant and less than 0.001 ( $**P < 0.001$ ) was considered high statistically significant. All statistical calculations were done using computer program SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL USA) version 20 for Microsoft Windows (2010).

### **3. Results**

#### **Baseline Characteristics**

Patient baseline characteristics were generally similar across the all groups (**table 1**). There were no statistically significant differences in demographic data among the five groups.

#### **Types of outcome measures**

##### **1. Time to recovery of the TOF ratio to 0.9 using acceleromyography.**

Group A patients have been achieved TOF 0.9 after administration of neostigmine 0.05 mg/kg as a reversal drug at TOF 0.2 by a mean time of 213.1 seconds and a SD  $\pm 48.8$ , while patient of group B when sugammadex 3mg /kg used as a reversal drug also at TOF 0.2 they achieve TOF 0.9 by a mean time of 78 seconds and a SD  $\pm 16.75$  which is high significant difference decrease with a *P* value  $< 0.001$ . Groups C and D patients the dose of sugammadex as a reversal drug was 3mg/kg and 6 mg/kg respectively resulting in a mean time of 126.8 seconds and SD  $\pm 26.86$  in group C and a mean time of 84.75 seconds and SD  $\pm 17.05$  in group D which is high significant decrease in time with a *P* value  $< 0.001$ . Patients of group E duplication of rocuronium dose and duplication of sugammadex dose than that of group D patients, a mean time of 70.5 seconds and a SD  $\pm 8.56$  was recorded which is less than group D patients without significant difference with a *P* value 0.103 (**table 2**), (**fig.1**). No statistical significant in the recovery time with the patients of the same group with the same dose of sugammadex as regard the different PTC stimulation (**table 5**).

**Table (1): Distribution of the studied patients regarding their demographic data:**

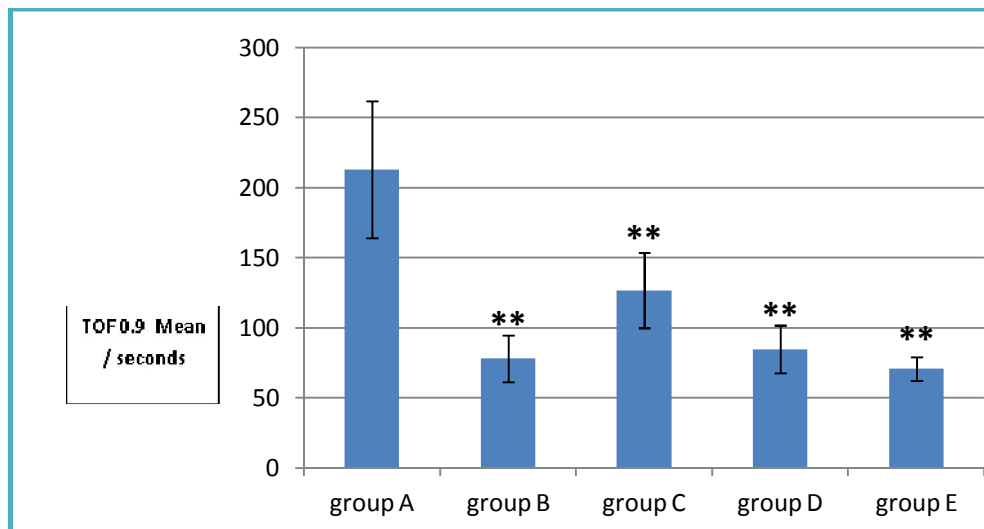
	Groups					Test of significance	P value
	A (n=20)	B (n=20)	C (n=20)	D (n=20)	E (n=20)		
<b>Age (year)</b> Mean ±SD	32.3 ±5.7	30.00 ±4.9	30.2 ±5.59	30.4 ±5.6	29.5 ±5.35	F=0.777	0.543
<b>Weight (kg)</b> Mean ±SD	68.65±11.4	68.3 ±13.09	67.7 ±9.02	66.6 ±9.32	63.9 ±9.62	F= 0.645	0.632
<b>Height (cm)</b> Mean ±SD	170.2±6.49	167 ±7.26	166.2±6.82	163.2±6.87	159.3±5.41	F=1.388	0.244
<b>BMI</b> Mean ±SD	24.12±2.54	24.3± 3.19	24.34±2.25	23.68±2.58	20.51±1.7	F=0.677	0.614
<b>Sex</b>	No. (%)	No. (%)	No. (%)	No. (%)	No. (%)		
<b>Male (no=60)</b>	14 (70)	15 (75)	10 (50)	10 (50)	11 (55)		
<b>Female(no=40)</b>	6 (30)	5 (25)	10 (50)	10 (50)	9 (45)	$\chi^2=4.583$	0.333

\* P-value < 0.05 (statistically significant) \*\*P < 0.001 (statistically high significant)

**Table (2): Distribution of the five groups regarding their achievement TOF 0.9 after reversal (Seconds)**

Motor block (seconds)	Groups					F test	Post hoc value: (LSD ** p value)
	A (n=20)	B (n=20)	C (n=20)	D (n=20)	E (n=20)		
	Mean ±SD	Mean ±SD	Mean ±SD	Mean ±SD	Mean ±SD		
<b>TOF 0.9</b>	213.1 ±48.8	78.00 ±16.75	126.8 ±26.86	84.75 ±17.05	70.5 ±8.56	93.538  P <0.001*	<0.001 (A,B)* <0.001 (A,C)* <0.001 (A,D)* <0.001 (A,E)* <0.001 (B,C)* 0.437 (B,D) 0.388 (B,E) <0.001 (C,D)* <0.001 (C,E)* 0.103 (D,E)

\* P-value < 0.05 (statistically significant) \*\*P < 0.001 (statistically high significant) LSD: least significant difference between each group



\* P-value < 0.05 (statistically significant) \*\*P < 0.001 (statistically high significant)

**Fig (1): Distribution of the five groups regarding their achievement TOF 0.9 after reversal (Seconds)**

**Table (3): post reversal mean arterial pressure (mmHg) among of the groups**

MAP (mmHg)	Groups					F test	P value
	A (n=20)	B (n=20)	C (n=20)	D (n=20)	E (n=20)		
Baseline	90.85 ± 5.1	88.8 ± 4.87	90.5 ± 4.21	88.1 ± 5.30	88.55 ± 4.98	1.261	0.291
1 min	90.95 ± 4.95	88.8 ± 4.87	90.4 ± 4.12	88.2 ± 5.25	87.9 ± 4.81	1.584	0.186
2 min	92.8 ± 5.5	89.45 ± 5.84	90.45 ± 4.93	87.0 ± 6.92	87.05 ± 5.57	3.396	0.009*
5 min	93.01 ± 4.94	89.4 ± 6.15	90.25 ± 4.8	86.2 ± 6.45	87.20 ± 5.45	4.124	0.002*
10 min	92.25 ± 4.26	89.3 ± 5.82	91.1 ± 3.62	86.4 ± 5.41	87.35 ± 5.15	4.492	0.002*
20 min	92.25 ± 4.26	89.3 ± 5.27	91.35 ± 3.57	87.75 ± 5.41	87.45 ± 4.9	3.798	0.004*
30 min	91.55 ± 4.87	89.4 ± 4.94	90.25 ± 5.13	87.85 ± 5.65	87.4 ± 4.84	2.746	0.023*

\* P-value < 0.05 (statistically significant) \*\*P < 0.001 (statistically high significant)

The statistically significant values is this table pointing to the changes in mean arterial blood pressure within a group and in the same time in comparing with the other groups.

**Table (4): Post reversal pulse rate (beat /min) among the groups**

MAP (mmHg)	Groups					F test	P value
	A (n=20)	B (n=20)	C (n=20)	D (n=20)	E (n=20)		
Baseline	81.60 ± 7.52	80.65 ± 7.11	80.40 ± 4.07	80.7 ± 6.13	79.55 ± 7.14	0.266	0.899
1 min	81.95 ± 7.53	80.65 ± 7.12	80.5 ± 4.05	80.45 ± 6.21	79.6 ± 7.16	0.334	0.855
2 min	90.95 ± 9.2	87.35 ± 10.60	80.61 ± 5.36	78.51 ± 9.12	76.05 ± 5.96	10.5	<0.001**
5 min	88.05 ± 10.21	83.9 ± 11.62	78.25 ± 6.64	75.45 ± 7.61	74.10 ± 5.91	9.697	<0.001**
10 min	83.75 ± 9.54	78.3 ± 11.31	75.55 ± 5.71	73.35 ± 6.75	71.70 ± 5.09	6.75	<0.001**
20 min	78.35 ± 5.65	74.45 ± 7.25	73.40 ± 4.97	74.5 ± 6.85	70.55 ± 6.07	4.074	0.003*
30 min	77.01 ± 5.41	72.9 ± 5.36	72.7 ± 5.01	74.09 ± 6.81	70.45 ± 6.05	3.641	0.008*

\* P-value < 0.05 (statistically significant) \*\*P < 0.001 (statistically high significant)

The statistically significant and high significant values is this table pointing to the changes in pulse rate within a group and in the same time in comparing with the other groups.

**Table (5) Comparison of the Mean and SD of post recovery time between Group C and D as Regarding their PCT**

PTC	Groups		F test	P value
	C(n=20)	D(n=20)		
0-1	131.78 ± 20.53	88.75 ± 14.93	1.819	0.176
2-3	125.00 ± 31.22	81.41 ± 19.08		
4-6	100.00 ± 43.31	60.00 ± 00.00		

\* P-value < 0.05 (statistically significant) \*\*P < 0.001 (statistically high significant)

2. Prevalence of postoperative residual neuromuscular blockade (or recurrence of blockade), defined and confirmed as train-of-four (TOF) ratio < 0.9 in acceleromyography.

All patients' tracheas were extubated promptly once neuromuscular function had returned (TOF 0.9), and no patient had evidence of residual or re-curarization through continuing neuromuscular monitoring after the injection of sugammadex, or clinically during patients' stay in the recovery room all over the observation period.

3. Monitoring of noninvasive mean arterial pressure (MAP) and heart rate (HR)

Immediately before and after the administration of the reversal drugs and subsequently at 2, 5, 10, 20 and 30 minutes (table 4) (table 5).

4. Prevalence of complications secondary to sugammadex.

In addition, oxygen saturation, respiratory frequency, and clinical evidence of residual curarization evidence or re-curarisation were



monitored after recovery of the T4/T1 ratio to 0.9 and for 60 minutes also side effects were recorded.

The adverse events reported with the use of sugammadex were minor and transient as one case report dizziness with a dose of 6 mg/kg in group D, one case had irritability with a dose of 12 mg/kg in group E (have been investigated and the reason was undeclared family problem), 2 cases had mild cough that lasted less than 2 minutes with a dose of 3 mg/kg in group C and resolved spontaneous without active management, 2 cases got a 10% decrease MAP and lasted less than 10 minutes with a dose of 6 mg/kg in group D and resolved spontaneous without active management, 3 cases had increased HR that were resolved spontaneously within 10 minutes without active management in group B, 2 cases had increased mandibular muscle tone for less than a minute one of them with a dose of 3 mg/kg in group B and the second with a dose of 3mg/kg in group C which

resolved spontaneous without active management (table 5).

Sugammadex was not associated with dry mouth in the post anesthesia care unit. There was no apparent relation between the sugammadex dose and the incidence of adverse events as has been listed in table 5, and there were no discontinuation due to occurrence of any adverse events during injection of sugammadex in either group.

Compared to neostigmine with atropine in group A adverse events reported was 2 cases had dry mouth, 2 cases had dizziness, 2 cases had 10% increased in MAP that resolved spontaneously without active management within 10 minutes, 7 cases had increased HR that were resolved spontaneously without active management and one case had post-operative nausea that resolved with reassurance within 20 minutes without active management, no cases report reoccurrence of neuromuscular blockade or residual neuromuscular blockade (table 5).

**Table (6): Side effects and percentage of its incidence among the five groups**

<i>Side Effects</i>	<i>Group A No (%)</i>	<i>Group B No (%)</i>	<i>Group C No (%)</i>	<i>Group D No (%)</i>	<i>Group E No (%)</i>
<b>Dry mouth</b>	2 (10)	0 (0)	0 (0)	0 (0)	0 (0)
<b>Dizziness</b>	2 (10)	0 (0)	0 (0)	1 (5)	0 (0)
<b>Dysrhythmia</b>	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
<b>MAP (increased)</b>	2 (10)	0 (0)	0 (0)	0 (0)	0 (0)
<b>MAP (decreased)</b>	0 (0)	0 (0)	0 (0)	2 (10)	0 (0)
<b>H.R (increased)</b>	7 (35)	0 (0)	0 (0)	0 (0)	0 (0)
<b>H.R (decreased)</b>	0 (0)	3 (15)	0 (0)	0 (0)	0 (0)
<b>PONV</b>	1 (5)	0 (0)	0 (0)	0 (0)	0 (0)
<b>Allergy</b>	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
<b>Cough</b>	0 (0)	0 (0)	2 (10)	0 (0)	0 (0)
<b>IMT</b>	0 (0)	1 (5)	1 (5)	0 (0)	0 (0)
<b>Irritability</b>	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)
<b>Residual block</b>	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

#### 4. Discussion

The  $\gamma$  – cyclodextrin derivative sugammadex is a novel agent used to selectively reverse the action of rocuronium and other steroidal non-depolarizing neuromuscular blocking agents (11). This study examines the evidence regarding the safety and efficacy of sugammadex in reversing neuromuscular blockade caused by rocuronium in adults. The neuromuscular measurements were performed using objective “quantifiable” end points (i.e., acceleromyography data captured in real-time on a laptop computer) under identical anesthetic conditions.

The dosages of the anticholinesterase and anticholinergic drugs used in this study were the standard recommended doses. It is also important to point out that the reversal drugs were administered during general anesthesia with isoflurane, which has

well-known depressant effects at the neuromuscular junction. Isoflurane was used in combination with fentanyl at induction time with no additional narcotic or any other depressant drugs to facilitate a rapid emergence from anesthesia and to allow for the early clinical assessment of the patients’ muscle strength.

This study a one hundred patients was divided randomly in five equal groups and was conducted from March 2015 to February 2016; group A and group B patient received rocuronium is a dose of 0.6 mg/kg and the reversal drug (neostigmine in group A and sugammadex 3mg/kg in group B) administration was at the end of surgery while TOF ratio is 0.2 to compare the time to recovery between neostigmine in standered dose and sugammadex 3 mg/kg. Patient of group C and D, the rocuronium dose was also 0.6 mg/kg and the reversal drug (sugammadex 3mg/kg in

group C and 6mg/kg in group D) administration was at the end of surgery while TOF ratio is still 0.0 with recording of PTC immediately before reversal time to compare the time to recovery with increasing the dose of sugammadex.

Patient of group E, the rocuronium dose was 1.2 mg/kg and the reversal drug (sugammadex 12 mg/kg) administration was at the end of surgery while TOF ratio still 0.0 with recording of PTC immediately before reversal time, to study the rapidity and completeness of reversing the neuromuscular effect of 1.2mg/kg rocuronium. In the meantime assessing the effectiveness of the rocuronium-sugammadex paradigm in RSI and replacing suxamethonium, as well as the safety of sugammadex in the all four groups comparing to the reversal with neostigmine (the standard drug for reversal of neuromuscular block).

The times from administration of sugammadex for patient of group C (17 patients out of the 20 had PTC 0-2 and only 3 patient had PTC 5-6) in a dose of 3 mg /kg to recovery of TOF ratio  $\geq 0.9$  was 2.11 minutes with no statistical significant value in the time of recovery as regard the different PTC; while for patients of group D (18 patients had PTC 0-2 and one patient had PTC 6 and one patient had PTC 3), the time was only 1.41 minute with no statistical significant value in the time of recovery as regard the different PTC in agreement with the study of R. M. Williamson, S. Maalaiah and P. Barclay in 2011, as they found no correlation between PTC at administration of sugammadex and time to TOF ratio 90% using sugammadex in a dose of 4 mg/kg to reverse 1.2 mg/kg rocuronium in the patients of their study (12).

When sugammadex was used for reversal of 1.2 mg/kg rocuronium with a TOF ratio 0.0 (all patient of this group had PTC 0) with a dose of 12 mg /kg in patients of group E the time was only 1.15 minute to full recovery and a TOF ratio achieved was  $\geq 0.9$ .

This study confirms the time of recovery to TOF 0.9 from profound neuromuscular block with sugammadex with increasing the dose of sugammadex, and the rapid recovery with a dose of 12 mg/kg in reversing 1.2 mg/kg rocuronium, goes hand-in-hand with the observation of Lee et al. on 2009 confirming the efficacy of rapid reversal in cannot intubate, cannot ventilate (CICV) scenario as well as for RSI with capability to reverse the neuromuscular blockade at the end of surgery even short time ones with high efficacy and safety.

Ozlem in 2007 found no evidence of a hypotensive effect due to sugammadex when it was administered under steady-state anesthetic conditions. In fact the MAP and HR values remained stable during the entire post-reversal observation period (13). In

consistency with this study, this new reversal drug appears to be free of any clinically significant hypotensive effects. However, the statistically significant values that was detected as decrease in MAP in group D with no clinical effects on patients hemodynamic is considered of no clinical significant value.

Also the decreased of HR in group B, C, D and E with no changes in MAP or patient hemodynamic effects considered of no clinical significant value and also the recorded pulse rates still within normal HR values, meanwhile the patient status change from light plan of general anesthesia immediately before reversal to full recovery after sugammadex and pain free because of the analgesic effect of fentanyl specially in group C, D and E is considered a reason for that decrease; so this decrease in HR even it is of no clinical significant could not proved as an effect of the reversal agent sugammadex. While 7 patients of group A (35%) their heart rate was increased within 2 minutes of reversal and was high statistically significant values as the increase rate was more than 15% of the basal value in some cases.

Compared to the standard cholinesterase-inhibiting drug (neostigmine), sugammadex was associated with a more rapid and complete reversal from rocuronium-induced neuromuscular block under general anesthesia. The use of sugammadex also obviated the need for the anticholinergic drugs as it should be used with cholinesterase-inhibiting drug (13). These comparative data suggest that when steroid based nondepolarizing neuromuscular blocking drugs such as rocuronium is used to facilitate tracheal intubation for short surgical procedures, the availability and the use of sugammadex may provide a more rapid and complete reversal of residual blockade at the end of surgery regardless the time of reversal and / or the degree on neuromuscular block.

## Conclusion

sugammadex was safe and well tolerated when used to reverse the neuromuscular block induced by rocuronium in a reverse pattern that means increasing the dose of sugammadex from 3 mg/kg to 6 mg/kg decreasing the recovery time from 2.1 minutes to 1.4 minute approaching only 66% of the time of the low dose. A dose of 3 mg/kg sugammadex, a high significant difference decrease in the time of recovery in comparing with neostigmine 0.05 mg/kg as the recovery time decreased from 3.55 minutes to 1.3 minutes is approaching only 30% of neostigmine time.

The potential benefits of sugammadex in terms of increased patient safety, increased predictability of recovery from NMB, minimizes the risk of residual block or reoccurrence of neuromuscular block and its consequences, promotes a rapid turnover of patients in

the operating theaters and more efficient use of theatre time and staff, which is cost-effective and limits the disadvantage of its high cost; as well its advantage in situations such as a “CICV” specially in RSI cases, together with its use when suxamethonium is contraindicated have led the consideration of sugammadex is the ideal reversal agent and is likely to be used more in the future.

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