Turk J Anaesthesiol Reanim 2016; 44: 206-11 DOI: 10.5152/TJAR.2016.97720

Original Article

Effect of Smoking on Reversing Neuromuscular Block

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Abstract

Objective: Rocuronium is a non-depolarising, intermediate-acting, monoquaternary amino steroid and was brought into clinical use as a potentially ideal muscle relaxant. Post-operative residual curarisation (PORC) results from the prolonged effects of non-depolarising neuromuscular blocking agents. This is a common problem and seriously affects patient safety. No recent study has investigated the effects of sugammadex on smokers, which is often used to restore neuromuscular block and avoid PORC. This study compares the severity of the effects of sugammadex used for antagonising rocuronium bromide and antagonism durations in smokers and non-smokers.

Methods: This randomised, prospective study included 40 patients scheduled for elective surgery and belonging to classes I and II based the American Society of Anesthesiologists classification, who were either smokers for at least 10 years or non-smokers. Patients underwent routine and neuromuscular monitoring. At induction, 2 mg kg^{-1} propofol and 1 mcg kg^{-1} intravenous fentanyl were applied. After the loss of eyelash reflex, 0.6 mg kg^{-1} intravenous rocuronium was administered. Patients were intubated at train of four (TOF) 2. Anaesthesia was continued with 50% O_2+50% air and 2% sevoflurane. Rocuronium, 0.15 mg kg^{-1}, was administered at TOF 2 during the operation. At the end of the operation, 2 mg kg^{-1} sugammadex was administered. The times until TOF 0.7, 0.8 and 0.9 were recorded.

Results: Intubation time was 132.8±46.4 s for smokers and 127.6±32.7 s for non-smokers. After sugammadex administration, the time to TOF 0.7 was 153.3±54.7 s in smokers and 125±67.2 s in non-smokers. The times were 178.4±58.8 and 146.6±72.6 s for TOF 0.8 and 200.8±55.8 s and 170.4±77.8 s for TOF 0.9 in smokers and non-smokers, respectively.

Conclusion: Although not statistically significant, the time to reach each TOF was longer for smokers. Larger populations and different perspectives are needed to find if sugammadex use is affected by smoking, which has negative effects on the body.

Keywords: General anaesthesia, sugammadex, smoking

Introduction

Neuromuscular blockers used for intubation and muscle relaxation play an important role in general anaesthesia. Rocuronium is a muscle relaxant used for this purpose. It is a non-depolarising, intermediate-acting, monoquaternary amino steroid and was introduced in clinical settings as a potentially ideal muscle relaxant (1). Post-operative residual curarisation (PORC) results from the prolonged effects of non-depolarising neuromuscular blocking agents. This remains a common problem and seriously affects patient safety (2).

Currently, cholinesterase inhibitor agents are widely used in combination with muscarinic antagonists for decurarisation. However, cholinesterase inhibitors are ineffective in reversing the profound neuromuscular block. Furthermore, undesirable cardiovascular, respiratory and cholinergic side effects of these drugs are very common (3, 4). In recent years, sugammadex has been used for the decurarisation of the neuromuscular block brought about by steroidal neuromuscular blockers as an alternative to cholinesterase inhibitors. Sugammadex has a structure similar to that of modified γ-cyclodextrin (5, 6).

Tobacco use is a public health problem with a high priority worldwide. Nicotine in cigarettes is an alkaloid that has an agonist effect on nicotinic-cholinergic receptors. Chronic tobacco use leads to an increase in the concentration of nicotine in the blood. High blood nicotine level leads to a reduction in the number of nicotinic receptors (7, 8). Literature shows that the properties of the neuromuscular block can affect the use of perioperative neuromuscular blockers, the restoration of

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Received : 03.03.2016
Accepted : 17.05.2016

the neuromuscular block, and the assessment of PORC risk. No recent study has investigated the effects of sugammadex on smokers, which is commonly used to restore neuromuscular block and avoid PORC. This study hypothesises that the effectiveness of sugammadex varies between smokers and non-smokers.

Methods

The ethics committee approval was obtained from the Duzce University Ethics Committee along with informed consent from patients. The patients' age range was 18-60 years; they were scheduled for elective surgery and belonged to groups 1 and 2 based on the American Society of Anesthesiologists classification. A total of 40 patients [20 smokers (Group S) and 20 non-smokers (Group NS)] were included in the study. Group S included patients who smoked at least 10 packs or had been smoking for at least 10 years and were currently smoking, whereas Group NS included patients who had never smoked.

Patients were excluded from the study if during preoperative evaluation the cases had neuromuscular diseases (e.g. myasthenia gravis, myotonic dystrophy, motor neuron disease), undergone radiotherapy or chemotherapy, liver or renal diseases, disturbances in electrolyte balance, history of drug use affecting neuromuscular transmission, body mass index (BMI) more than 27 and alcohol use. Patients were also excluded from the study if they had post-operative complications such as surgical bleeding, haemodynamic instability, chest trauma, cerebrovascular events or hypothermia, which may prolong the duration of extubation.

The patients were asked not to smoke or eat 8 hours before surgery. Before surgery, patients were taken to the premedication hall, and vascular access was made with a cannula of 18 G in the antecubital region. A 0.9% NaCl infusion was administered at a rate of 8-10 ml kg^{-1} hr^{-1}. Premedication was provided by applying 0.03 mg kg^{-1} of intravenous (IV) midazolam for 30 min before surgery.

For cases taken to the operation room, a Datex-Ohmeda S/5 device was used to monitor ECG (DII derivation), peripheral oxygen saturation (SpO_2), non-invasive arterial blood pressure, respiratory rate, end-tidal carbon dioxide ($ETCO_2$) and inspiratory sevoflurane concentrations. For vascular measurements, a blood pressure cuff was applied to one arm, and the other arm was used for neuromuscular monitoring. The Datex-Ohmeda S/5 device was also used for monitoring neuromuscular transmission.

Once the skin was cleaned and dried with an alcohol swab, the distal electrode was placed 1 cm above the wrist joints on the ulnar nerve, which is next the ulnar artery on the volar side of the wrist (Neotrode® Neonatal ECG Electrode, USA). The proximal electrode was placed on the skin 2-3 cm proximal to the distal electrode. The acceleration transducer was mounted on the thumb with a finger adapter, and the hand was fixed to the operation table without its thumb. The skin temperature of the hand was measured through neuromuscular monitoring and was ensured to be above 33°C.

Heart rate, systolic arterial pressure, diastolic blood pressure, mean arterial pressure and SpO_2 values were recorded by measuring at 5 min intervals before, during and after the operation. All patients received 3 min of pre-oxygenation with 100% oxygen. At induction, 2 mg kg^{-1} of propofol and 1 μg kg^{-1} of IV fentanyl were administered. After the loss of eyelash reflex, the neuromuscular monitoring module of the Datex-Ohmeda S/5 device was set to give automatic supramaximal alerts. IV rocuronium was administered at a rate that would reach 0.6 mg kg^{-1} concentration within 5-10 s. Orotracheal intubation was carried out when the train of four (TOF) counter reached 2, starting with TOF stimulation at a frequency of 2 Hz at 10-s intervals and the pre-determined supramaximal alert. Endotracheal intubation was performed by the same anaesthesiologist, and the intubation quality was evaluated using the intubation scale as shown in Table 1 (9). A total score of 8-9 was considered to indicate excellent intubation, whereas 6-7 was considered good, 3-5 was considered weak and 0-2 was considered poor.

Train of four monitoring was continued with 5-min intervals. The intubation time (T2i) was recorded as the time passing until a TOF count of 2 was obtained after muscle relaxant application. The clinical effect duration (T2d) was recorded as the time until a TOF count of 2 was obtained after the maximum block following the muscle relaxant application. During the operation, 0.15 mg kg^{-1} of rocuronium was administered to the patient when the TOF counter reached 2. The Datex-Ohmeda S/5 anaesthesia device and a semi-closed loop system were used in both groups. The anaesthesia was maintained with 50% O_2+50% air and 2% sevoflurane. Ventilation parameters were set such that the $EtCO_2$ levels of the patients would be 30-35 mmHg.

At the end of the operation and at least 15 min after the last dose of rocuronium, 2 mg kg^{-1} of sugammadex was administered. The time to reach TOF values of 0.7, 0.8 and 0.9 were recorded. The patient was extubated when the TOF value was 0.9. The cases were taken to the wake-up room, where monitoring was continued for 30 min. The patients with no follow-up problems were sent to the service.

Statistical analysis

The statistical software package Statistical Package for the Social Sciences 10.0 for Windows (SPSS Inc; Chicago, IL, USA) was used for analysis. The independent t-test and chi-square test were used for comparisons. Based on the literature and clinical information, a change of ±2 min in the time to reach a TOF value of 0.9 was thought to be important, and it is thought that 20 subjects would be enough for Group S and Group NS to achieve 80% test reliability and a 5% chance of type I error. Because the time to reach TOF 0.9 was de-

termined as the major criteria, the minimum sample size was determined by that time, and significance was determined by $p<0.05$. All values are expressed as mean±standard deviation. Qualitative data were analysed using a chi-square test. Non-parametric data were analysed using the analysis of variance or Mann-Whitney U test. Parametric quantitative data were analysed using paired t-test. Because both parameters were normally distributed, the correlation coefficients and their significance were calculated using the Pearson test. A p-value of ≤0.05 was deemed significant.

Results

No statistically significant difference was found between groups in terms of age, BMI, sex, operation time and body temperature during the operation (Table 2). No statistically significant difference was found in comparing the dose of rocuronium and the duration between the last rocuronium dose and sugammadex administration between the groups (Table 3).

Although the intubation time was found to be 127.6 s in Group NS and 132.8 s in Group S, the difference was not statistically significant.

The first time that rocuronium was needed was found to be 35.1 min in Group S and 36.3 min in Group NS (with no statistical significance). The time to reach TOF 0.7 measured after 2 mg kg^{-1} of sugammadex was administered was 153.3 s in Group S and 125 s in Group NS, whereas it was 178.4 s in Group S and 146.6 s in Group NS for TOF 0.8, and 200.8 s in Group S and 170.4 s in Group NS for TOF 0.9. Although the time to reach TOF 0.9 was longer in Group S compared to that in Group NS, the difference was not statistically significant (Table 4).

Discussion

Sugammadex usage added a shorter and safer recovery profile in daily clinical anaesthesia practice. Furthermore, it was proved by several clinical studies in humans (5, 6). Lu et al. (10) reported that 2 mg kg^{-1} of sugammadex usage is adequate for effective and rapid neuromuscular recovery. In the present study, we ensured a safe and rapid recovery profile using the same dose.

Abad-Gurumeta et al. (11) reported that sugammadex reduced residual paralysis risk, respiratory adverse events, post-operative vomiting ratio according to neostigmine.

After the use of sugammadex as a reversal agent and rocuronium as a neuromuscular blocking agent, the time to reach TOF 0.7, 0.8 and 0.9 in relation to intubation time and the total dose of rocuronium were compared in smokers and non-smokers. No statistically significant difference was found. Cigarette consumption remains one of the main health problems worldwide. An excessive smoking habit is defined as smoking at least 24 cigarettes per day for more than 10 years (12). Chronic cigarette smoking has negative impacts on respiratory, circulatory and other systems. It affects hepatic drug metabolism by causing enzyme induction and can alter the pharmacodynamics of various drugs (13). Contradictory results have been obtained in previous studies investigating the effects of tobacco use on neuromuscular agents.

Teiria et al. (14) compared the vecuronium doses in smokers and non-smokers and noticed an increase of 25% in vecuro-

Table 1. Cooper scale used for intubation (9)

Score jaw relaxation	Vocal cords	Response to intubation	Score
Poor (impossible)	Closed	Severe coughing or bucking	0
Minimal (difficult)	Closing	Mild coughing	1
Moderate (fair)	Moving	Slight diaphragmatic movement	2
Good (easy)	Open	None	3

Table 2. Patient characteristics

	Smoker (Group S) (n=20)	Non-Smoker (Group NS) (n=20)	p
Age (year) *			
Mean±SD	38.8±8.5	36.4±11.3	0.445
Body mass index (kg/m^2)*			
Mean±SD	22.8±1.3	23.0±2.2	0.770
Gender (%)**			
Female	6 (42.9%)	8 (57.1%)	0.507
Male	14 (53.8%)	12 (46.2%)	
Operation time (min)*			
Mean±SD	128±3.1	120±31	0.436
Body temprature (°C)*			
Mean±SD	35.6±0.47	35.8±0.48	0.089

*Independent t-test was performed. SD: standard deviation

Table 3. Comparison of the total dose of rocuronium and the duration between the last rocuronium dose and sugammadex administration (Rss) between the groups

	Group S	Group NS	p
Total Rocuronium (mg)	77.9±12.9	77.1±17.8	0.872
Rss (min)	19.4±3.8	21.5±5.3	0.164

*Mann–Whitney U test was performed

Table 4. Comparison of the TOF times between groups

	Group S	Group NS	p
T2i (s)	132.8±46.4	127.6±32.7	0.685
T2d (min)	35.1±9.4	36.3±12.8	0.738
TOF 0.7 (s)	153.3±54.7	125±67.2	0.153
TOF 0.8 (s)	178.4±58.8	146.6±72.6	0.136
TOF 0.9 (s)	200.8±55.8	170.4±77.8	0.165

*Mann–Whitney U test performed

nium maintenance dose after reduction in the clinical effect range of vecuronium. They explained this situation with the change in the hepatic metabolism of vecuronium and the receptor level. Rautoma et al. (15) studied the effect of smoking on rocuronium. They concluded that smokers need more rocuronium with the same anaesthesia and that neuromuscular block should be controlled constantly to avoid insufficient neuromuscular block, which may affect the surgical team. They attributed the study results to the high metabolism of the smokers. In the present study, the total rocuronium needed was found to be similar in groups where the operation time was not statistically different.

Pühringer et al. (16) found that smoking does not change the dose requirement or the pharmacodynamics of rocuronium. Salihoğlu et al. (17) discovered a decrease of 25% in the neuromuscular effect of rocuronium, starting time and recovery time in smokers compared with non-smokers. They attributed this to the decrease in the number of the nicotinic receptors caused by the chronic nicotine use. Compared with Group S, the onset of the neuromuscular blocking effect of rocuronium was shorter in Group NS in the present study; however, the results were not statistically significant. We attributed this difference to the small sample size of the present study. However, authors must consider the possibility of another molecular mechanism instead of the down regulation of nicotinic receptors.

Latorre et al. (18) examined the effect of smoking on neuromuscular transmission following rocuronium administration in 40 individuals. They concluded that smoking does not affect the drug's pharmacokinetics and pharmacodynamics. In our study, patients were divided into groups: 20 smokers and 20 non-smokers. Although the intubation time of non-smokers was shorter than that of smokers, it was not statistically significant. The first time when rocuronium was needed was the same in both groups.

Post-operative residual curarisation is defined as the presence of nicotinic receptors that remain blocked in a patient. A total of 60%-70% of receptors are known to remain curarised, even when this situation causes no symptoms (19). One of the most important factors affecting mortality and morbidity is PORC (20, 21). As long as neuromuscular monitoring at the adductor pollicis muscle does not indicate a TOF of 0.90 or higher, normal vital muscle functions and normal breathing are not guaranteed (22).

When carrying out post-operative evaluation, factors that affect the clinical improvement of patients should be taken into consideration. Volatile anaesthetic blood subjected to long-term exposure can exist at high concentrations in a few tissues, and it should be kept in mind that its disposal from the body can take a long time. Thus, together with the sedative effects, the inhaled anaesthetics' neuromuscular blocking constructive effects may occur in the post-operative period (21, 23, 24).

The effectiveness and action duration of the drugs that create non-depolarising neuromuscular block may vary depending on sex, and some studies indicate that the action duration of these drugs is longer in women (25, 26). However, there was no sex-specific difference observed between the groups in our study.

Anaesthetic technique does not affect the pharmacokinetics of rocuronium. However, age has shown to impact pharmacokinetics (27). As a result of the reduction in body fluids with advancing age (particularly extracellular volume reduction) and insufficient organ function, the pharmacokinetics of rocuronium are affected, and the rate of drug elimination decreases. False results obtained due to age were eliminated by examining the same age groups.

Body temperature is one of the most important factors that affects the recovery of neuromuscular functions (28). Feldman et al. (29) suggested that the separation of non-depolarising muscle relaxants from the receptor is prolonged by a low body temperature because of the decreased release of acetylcholine during hypothermia. Body temperatures were measured during operation, and the peripheral body temperature was above 33°C. There was no difference between groups in terms of body temperature.

Sugammadex is the first selective neuromuscular blocking agent used for reversing the effect of neuromuscular blocking agents. The decurarisation provided by sugammadex is a new approach for a fast and safe reversal of neuromuscular block as opposed to using rocuronium or vecuronium (30). By creating a 1-1 inclusion complex with the steroidal muscle relaxants, the effects of these drugs are terminated. The drug combines with free rocuronium and reduces the concentration of the free form. It creates a concentration gradient between this nerve-muscle junction and the central compartment (plasma and extracellular fluid). As rocuronium moves from the neuromuscular junction to the plasma, it is encapsulated with sugammadex, and the neuromuscular block is quickly terminated. It has no effect on acetylcholine. There remains no need for anticholinergics; therefore, their side effects can be avoided (31).

Sorgenfrei et al. (32) examined the dose-response relationship, safety and pharmacokinetics of sugammadex. They found that a sugammadex dose of 2 mg kg^{-1} and above is safe. In our study, no side effects related to sugammadex were observed. Blobner et al. (33) administered 2 mg kg^{-1} of sugammadex or 50 µg kg^{-1} of neostigmine (a conventional method) to the patients who were already administered rocuronium in a randomised controlled study on 198 patients. The time to reach TOF 0.9 was 1.4 min in the sugammadex group and 17.6 min in the neostigmine group.

Conclusion

Smoking is known to alter the effects of neuromuscular agents and recovery times of the patients. It is believed that studies with larger populations and different perspectives are needed to evaluate sugammadex use with smoking, which has negative effects on all body systems.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Düzce University School of Medicine (2012/254).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - Ö.Ö.; Design - Ö.Ö., G.Y.S.; Supervision - O.Ö., Y.D.; Resources - Ö.Ö., B.D.; Materials - H.A.; Data Collection and/or Processing - Ö.Ö.; Analysis and/or Interpretation - Y.D., H.A.; Literature Search - H.A.; Writing Manuscript - Ö.Ö.; Critical Review - O.Ö., Y.D., H.A.; Other - Ö.Ö., B.D., H.A.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

References

1. Özcengiz D. Neuromuscular blockers. Türkiye Klinikleri J Anest Reanim 2005; 3: 116-30.
2. Naguib M, Kopman AF, Lien CA, Hunter JM, Lopez A, Brull SJ. A survey of current management of neuromuscular block in the United States and Europe. Anesth Analg 2010; 111: 110-9.
3. Kim KS, Lew SH, Cho HY, Cheong MA. Residual paralysis induced bye it her vecuronium or rocuronium after reversal with pyridostigmine. Anesth Analg 2002; 95: 1656-60. [CrossRef]
4. Flockton EA, Mastronardi P, Hunter JM, Gomar C, Mirakhur RK, Aguilera L, et al. Reversal of rocuronium-induced neuromuscular block with sugammadex is faster than reversal of cisatracurium-induced block with neostigmine. Br J Anaesth 2008; 100: 622-30. [CrossRef]
5. Sacan O, White PF, Tufanogulları B, Klein K. Sugammadex reversal of rocuronium-induced neuromuscular blockade: a comparison with neostigmine-glycopyrrolate and edrophonium-atropine. Anesth Analg 2007; 104: 569-74. [CrossRef]
6. Blobner M, Eriksson LI, Scholz J, Motsch J, DellaRocca G, Prins ME. Reversal of rocuronium-induced neuromuscular blockade with sugammadex compared with neostigmine during sevoflurane anaesthesia: results of a randomised, controlled trial. Eur j Anaesthesiol 2010; 27: 874-81. [CrossRef]
7. Taylor P. Agents acting at the neuromuscular junction and autonomic ganglia. In: Goodman Gilman A, Rall TW, Nies AS, Taylor P, (eds). The Pharmacological Basis of Therapeutics. New York, McGrawHill Inc., 1990; 166-86.
8. Ross EM. Pharmacodynamics: Mechanism of drug action and the relationship between drug concentration and effect. In: Goodman Gilman A, Rall TW, Nies AS, Taylor P, (eds). The Pharmacological Basis of Therapeutics. New York, McGrawHill Inc., 1990; 33-48.
9. Belekar VR, Khamankar S. Rocuronium for tracheal intubation in patients undergoing emergency surgery. Int J Pharmacol Res 2013; 3: 18-22.
10. Lu IC, Wu CW, Chang PY, Chen HY, Tseng KY, Randolph GW, et al. Reversal of rocuronium-induced neuromuscular blockade by sugammadex allows for optimization of neural monitoring of the recurrent laryngeal nerve. Laryngoscope 2016; 126: 1014-9. [CrossRef]
11. Abad-Gurumeta A, Ripollés-Melchor J, Casans-Francés R, Espinosa A, Martínez-Hurtado E, Fernández-Pérez C, et al. A systematic review of sugammadex vs neostigmine for reversal of neuromuscular blockade. Anaesthesia 2015; 70: 1441-52. [CrossRef]
12. Collins VJ, Preanesthetic evaluation and preparation InPrinciples of Anesthesiology, Collins VJ (ed), Lea&Febiger, Philadelphia, 1993; 207-52.
13. Dawson GW, Vestal RE. Smoking and drug metabolism. Pharmacol Ther 1982; 15: 207-21.
14. Teiria H, Rautoma P, Yli-Hankala A. Effect of smoking on dose requirements for vecuronium. Br J Anesth 1996; 76: 154-5. [CrossRef]
15. Rautoma P, Svartling N. Smoking increases the requirement for rocuronium. Can J Anaesth 1998; 45: 651-4. [CrossRef]
16. Pühringer FK, Keller P, Löckinger A, Kleinsasser A, Scheller A, Raedler C, et al. Smoking does not alter the dose-requirements and the pharmacodynamics of rocuronium. Can J Anaesth 2000; 47: 347-9. [CrossRef]
17. Salihoglu Z, Karaca S. Effects Of Smoking On Neuromuscular Blockade For Rocuronium. The Internet Journal of Anesthesiology 2007; 14: 1-4.
18. Latorre F, de Almeida MC, Stanek A, Kleemann PP. The interaction between rocuronium and smoking. The effect of smoking on neuromuscular transmission after rocuronium. Anaesthesist 1997; 46: 493-5. [CrossRef]
19. Morgan GE, Mikhail MS, Murray MJ. Neuromuscular blocking agent. In: Morgan GE, Mikhail MS. Murray MJ ed(s). Clinical Anaesthesiology. Newyork, Lange Medical Books/ McGraw-Hill Medical Publishing Division 2010: 179-98.
20. Shorten G.D. Postoperative residual curarisation (PORC): Incidence, etiology and associated morbidity. Anaesthesia and Intensive Care 1993; 21: 782-9.
21. Kayhan Z. Klinik Anestezi. Logos Yayıncılık Tic. A.Ş. Genişletilmiş 2. Baskı, Ankara, 1997; 135-60s.
22. Eriksson LI. Residual neuromuscular blockade; incidence and relevance. Anaesthesist 2000; 49: 18-9. [CrossRef]
23. Alver F, Evren Ç. Nöromusküler monitörizasyon: Anestezide Güncel Konular: Nobel Tıp Kitapevleri, 2002; s. 105-25.
24. Crul JF. Clinical aspects of rocuronium bromide. Data on file, Organon Teknika 1998 page I-II, 1-6, 19-26, 29-34, 37-42.

25. Tsai CC, Chung HS, Chen PL, Yu CM, Chen MS, Hong CL. Postoperative residual curarization: Clinical observation in the postanesthesia care unit. Chang Gung Med J 2008; 31: 364-8.
26. Parker CJ, Hunter JM, Snowdon SL. Effect of age, sex and anaesthetic technique on the pharmacokinetics of atracurium. Br J Anaesth 1992; 69: 439-43. [CrossRef]
27. McCoy EP, Maddineni VR, Elliott P, Mirakhur RK, Carson IW, Cooper RA. Haemodynamic effects of rocuronium during fentanyl anaesthesia: comparison with vecuronium. Can J Anaesth 1993; 40: 703-8. [CrossRef]
28. Bilgin F, Koçak T, Güler F, Oğuş H, Turan E, Erkılınç A, et al. Residual neuromuscular block with rocuronium on different hypothermic cardiopulmonary bypass conditions. Turk Goğus Kalp Damar Cerrahisi Dergisi 2003; 11: 66-71.
29. Feldman SA, Englan AJ, Margarson MP. Tracheal intubation conditions after one minute: Rocuronium and vecuronium alone and in combination. Anaesthesia 1997; 52: 336-40. [CrossRef]
30. Naguib M. Pharmacology of muscle relaxant and their rantagonist neuromuscular physiology and pharmacology. In: Miller RD (ed). Anaesthesia. 6th ed. Philadelphia, Churchil Livingston 2006: 481-572.
31. Srivastava A, Hunter JM. Reversal of neuromuscular block. Br J Anaesth 2009; 103: 115-29. [CrossRef]
32. Sorgenfrei IF, Norrild K, Larsen PB, Stensballe J, Ostergaard D, Prins ME, et al. Reversal of rocuronium induced neuromuscular block by the selective relaxant binding agent sugammadex a dose finding and safety study. Anaesthesiology 2006; 104: 667-74. [CrossRef]
33. Blobner M, Eriksson L, Scholz J, Hillebrand H, Pompei L. Sugammadex (2.0 mg/kg) significantly faster reverses shallow rocuronium-induced neuromuscular blockade compared with neostigmine (50 μg/kg). Eur J Anaesthesiol 2007; 24: 125. [CrossRef]