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Sugammadex Versus Neostigmine for Reversal of Rocuronium Induced Neuromuscular Blockade in Pediatric Patients Under General Anaesthesia

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Abstract: ***Background: Residual neuromuscular blockade (RNMB) is a common problem encountered in pediatric patients under general anesthesia with neuromuscular blockade, due to different physiological factors. To accelerate the reversal of neuromuscular blockade and to prevent RNMB, conventionally cholinesterase inhibitors are administered, and since these agents are not selective to nicotinic receptors and also stimulate the muscarinic system, they have multi-systemic side effects. For rapid effective reversal , and to eliminate the muscarinic side effects Sugammadex which is a novel selective relaxant binding agent introduced for reversal of neuromuscular blockade caused by aminosteroidal compounds like rocuronium, even from the deeper blockade. Aims and Objectives: This is a cross sectional study to compare the efficacy and safety of suggamadex and neostigmine for reversal of neuromuscular blockade in pediatric patients. The objective of study is to assess the quality of reversal using neostigmine and suggamadex by calculating mean extubation time and recovery time. Materials and Methods: A cross sectionl, randomised, double blinded, comparative study was conducted in king George hospital, vishakapatnam. Pediatric patients in the age group of 2-14years, ASA status 1and 2 Patients are randomly allocated in to two groups RN and RS are the patients receiving neostigmine and sugammadex for reversal. Results: Mean extubation time in group RS who received sugammadex is 103.25+25.54sec. Mean extubation time in group RN who received neostigmine is 212.05+60.41sec. P value <0.0001 showed a highly significant difference in mean extubation time between the two groups. Conclusion: The present study concluded that sugammadex is making faster and also safer reversal possible for an early extubation when compared with neostigmine in children, for the rocuronium induced neuromuscular blockade.***

1. Introduction

The importance of pharmacological reversal of neuromuscular blockade was suggested in 1945. Neuromuscular blocking agents are currently used during surgery to facilitatate muscle relaxation for endotracheal intubation and artificial ventilation.In 20- 40 % cases there are residual effects after surgery. There are few complications after NMB wich incude impaired respiration, laryngeal, pharyngeal functions, airway obstruction ,hypoxia and aspiration.

Residual neuromuscular blockade (RNMB) is more common in post operative period. RNMB may increase complications such as delayed recovery, pulmonary atelectasis, hypoxia, metabolic abnormalities and rarely death. To accelerate the reversal of neuromuscular blockade and to prevent RNMB, cholinesterase inhibitors like neostigmine are used. Since these cholinesterase inhibitors are not selective to nicotinic receptors and also stimulate the muscarinic system, they have multisystem side effects like bradycardia, bronchoconstriction, qt prolongation. Because of the above draw backs, there is a need of safe reversal agent.

NMB have different efficacy in adult and children. The inadequately mature neuromuscular junction in infants makes the ion channels remain open for a long time. Increased risk of postopresidual curarization is seen as a complication in pediatric patients due to the above physiological factors. The use of objective neuromuscular monitoring is considered more accurate and reliable compared with use of tactile or visual evaluation of muscle contraction response after stimulation by peripheral nerve stimulator. TOF monitoring is necessary for this study to provide objective assessment. Sugammadex is a novel cyclodextrin, first in a new class of selective relaxant binding agents,that reverse NMB with depolarizing muscle relaxants .

2. Aim and Objectives of the Study

This study is designed to compare the efficacy and safety of sugammadex and neostigmine for reversal of neuromuscular blockade in pediatric patients undergoing surgical procedures under general anesthesia

The primary objective of the study is to assess the quality of reversal using neostigmine and sugammadex by calculating mean extubation time. Also to calculate the recovery time from administration of the last dose of NMB to the appearance of T2 in TOF response, the extubation time from administration of the last dose of NMB to TOF ratio>0.9, and difference between these two parameters was taken as the mean extubation time as an indicator for efficacy of reversal agent. And for the safety profile of the reversal agent, we compare complications encountered in the recovery room.

3. Materials and Methods

A cross-sectional, randomized, double-blind, comparative study was conducted in King George hospital and government ENT hospital in Visakhapatnam with the approval from Institutional Scientific and Ethics Committee and after taking written & informed consent from all the patients or patient attendants. Eighty pediatric patients in the age group of 2 – 14 years of either sex belonging

to American society of Anaesthesiologists (ASA) physical status 1 and 2, scheduled for elective surgery under general anesthesia, comprised this study pool. This study was conducted between September 2018 to October 2019 in the Department of Anaesthesiology, King George Hospital, and Government ENT Hospital, Visakhapatnam. The sample size was based on literature. To detect a confidence interval of 95 %, a sample size of 40 patients in each group was calculated. To detect a statistical power of more than 99 % with an alpha error of 5%, it was estimated at 34 the required number of patients in each group, a totally of 68 patients. Adjusting for missing data, loss to follow up and non-compliance, the Sample size was increased to 80.

Patients who are of age group below two years and above 14, ASA grade 3 and above, BMI>40kg/m2, mentally retarded, deaf and dumb, with known drug hypersensitivity, neuromuscular disease or malignant hyperthermia, kidney failure or liver failure, and refused to participate in the study are excluded. Patients were randomly allocated into one of the two groups by computer-generated numbers.

Group RN: N=40 patients who receive neostigmine 0.05mg/kg for reversal.

Group RS: N = 40 patients who receive sugammadex 2mg/kg for reversal.

Patient was assessed as apart of PAC, 0.02mg/kg I.V.midazolam administered 30-45 min before surgery. In the OT Standard monitoring was attached, like Electrocardiogram (ECG), noninvasive blood pressure, pulse oxymetry, and capnograph for EtCO2 (End-Tidal CO2) monitoring (after intubation) for all the patients. The train-of-four (TOF) equipment working with the acceleromyometry principle (STIMPOD NMS450, XAVANT Technology, Pretoria, South Africa) was placed on the ulnar nerve course and transducer on the thumb of all the patients. An intravenous catheter was inserted on the arm opposite to the side of the neuromuscular monitoring. In both groups, induction of general anesthesia was done with 7 mg/kg thiopental 2microgram/kg fentanyl. The first TOF ratio of 100% calibrated and measured. 0.6 mg/kg rocuronium administered Intravenously. Ninety seconds after the first dose of rocuronium, the patients were orotracheally intubated, and the capnograph was attached for each patient — maintenance of anesthesia with 2% sevoflurane and 50% O2 - 50% N2O.

During the surgery, neuromuscular blockade was evaluated clinically according to the hemodynamic changes, an increase of respiration frequency, disruption to the respiratory curve, and the onset of muscular movements. When we get T1 in TOF, 0.2 mg/ kg rocuronium was administered, total doses of rocuronium were measured, and the point time of the last dose of NMB was recorded. Sevoflurane inhalation was interrupted at the end of surgery and switched to 100% Oxygen. The pediatric patients were randomly assigned to one of the two groups by a computer-generated table of random numbers. When T2 reappeared, Group RN (n = 40) received 0.01 mg/kg atropine and 0.05 mg/kg neostigmine and Group RS (n = 40) received 2 mg/kg sugammadex for the NMB reversal. After the reversal of NMB, gentle suction of secretions was carried out, and the patients were monitored clinically and with monitoring exhaled tidal volume for adequate tidal volume (>50% of normal) together with TOF monitoring till reappearance of T4 with fade no longer detected visually. Once after attaining TOF,> 0.9 patients were extubated. Time of administration of neostigmine or sugammadex after the last dose of NMB and the TOF ratio at the time of injection were recorded. Patients were clinically assessed for NMB recovery (50% of normal tidal volume, eye-opening, and limb movement) and extubated. Time from the reversal of NMB to extubation was measured as the extubation time. The TOF score at extubation and the time to reach TOF > 0.90 were recorded. Duration of surgery and anesthesia (time interval between induction and interruption of sevoflurane) were also recorded. Any complications such as bradycardia, hypotension, tachycardia, retching, vomiting, bronchospasm, laryngospasm, hypersalivation, coughing, diplopia, rash, fever, or dysgeusia were noted.

4. Statistical Analysis

To determine the association between the groups, comparison of qualitative variables was analyzed by chi-square test, and comparison of Quantitative variables was analyzed by Independent sample unpaired T-Test. A P - value of < 0.05 will be taken as level of significance. Data was presented as mean +/- S.D. Data was entered in Microsoft excel and Data analysis was performed using windows MEDCALC software.

5. Results

Demographic profile of study groups

Variable		Group RN (n=40)	Group RS (n=40)	p value	Significance
Age (years)		8.13 + 2.7	7.98 + 3.34	0.82	NS
Sex	Male	26 (65%)	24 (60%)	0.64	NS
	Female	14 (35%)	16 (40%)	0.64	NS
Weight (kgs)		20.2 + 6.79	21.1 + 10.2	0.64	NS
ASA Grade	I	31 (77.5%)	33 (82.5%)	0.57	NS
	II	9 (22.5%)	7 (17.5%)	0.57	NS

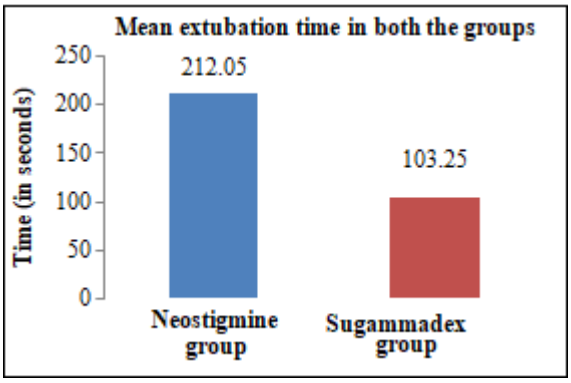
Evaluation of time variations in both groups

	Group RN	Group RS	P value	significance
Total duration of surgery	72.22	70.92	0.72	NS
Total duration of anesthesia	81.42	82.37	0.84	NS

Comparison of Recovery time and extubation time in both groups:

Time of Attainment	Group RN	Group RS	P Value	Significance
LAST NMB dose – Appearance of T2	1162.15 + 459.12	1099.67 + 458.64	0.54	NS
LAST NMB dose – TOF ratio > 0.9	1311.77 + 465.55	1265.6 + 466.20	0.65	NS

Mean extubation time
Group RN 212.05 + 60.41 sec
Group RS 103.25 + 25.54 sec
P value < 0.0001 highly significant



Complications encountered in both the groups

S.No.	Complication	Group RN (n=30)	Group RS (n=30)
1	Nausea	2	0
2	Vomiting	1	1
3	Upper airway obstruction	4	1
4	Skin rash	0	0
5	Bradycardia	0	0
6	Tachycardia	0	0
7	Hypotension	0	0
8	Dry mouth	3	0
9	Fever	1	1
10	Diplopia	0	0
11	Need for additional administration of reversal agent	0	0
12	Need for reintubation	0	0
13	Hypoxemia (<94%)	3	1
14	Laryngospasm	0	0
15	Bronchospasm	0	0
	Total complications	14	4

6. Discussion

Muscle relaxants are used during intra operative period to facilitate endotracheal intubation, ensure patient mobility, and improve surgical exposure. Reversal agents are used to terminate the action of muscle relaxants. The ideal reversal agent should have fast onset, should be efficient at any time, it should be able to provide complete reversal either for light or profound blockade. The ideal reversal agent is not yet existing, but sugammadex is cyclodextrin molecule which acts by encapsulation of rocuronium., it inactivates rocuronium by encapsulating the free molecule to form stable complex. Sugammadex exerts its effect by forming tight complexes at ratio 1:1 with aminosteriod muscle relaxants. The volume of distribution of sugammadex is proximately 18 L and volume of distribution at steady state is 11-14 L. The drug does not produce any metabolites and is mostly excreted through urine in unchanged form.

NMB have different efficacy in adults and children. Because of relatively large extracellular volume in children than in adults, the NMBAs create lower plasma concentrations in children. Higher doses of NMBA may be required to reach the same level of NMB in children, as in adults. The inadequately mature neuromuscular junction in infants makes the ion channels remain open for a longer time, and make the muscles can to be depolarized easily(.7). More type I fibrins in a child's diaphragm than an adult's, make it more vulnerable to blockade than the peripheral muscles. These physiological factors lead to an increased risk of curarization in pediatric patients.

Vuksanaj et al. investigated the pharmacokinetic properties of rocuronium in children. They stated that higher doses of rocuronium might be necessary for children for rapid onset and rapid recovery. It has been concluded that NMB reverses in a shorter time with rocuronium. Therefore, we preferred the use of rocuronium in our study (23) PORC is one of the feared complications after anesthesia. Since Beecher and Todd described a significant increase in mortality after the use of NMBA, the need for monitoring the effects of such drugs has been well recognized. The TOF stimulation pattern has been used since around 1970 to monitor residual neuromuscular blockade. However, over the past decade, the acceptable limit of TOF ratios has shifted from >0.7 to >0.9 due to significant pathology associated with shallow blockade.

The impact of residual neuromuscular blockade on respiratory complications beyond the acute recovery period has been previously reported by Berg et al. However, the authors found only cases of the severe residual blockade with TOF ratio <0.7 in combination with a long-acting NMBA to cause a sign depending on the muscle relaxant used, degree of spontaneous recovery, TOF ratios attained with standard doses of neostigmine, as well as the time for a satisfactory reversal of NMB, vary greatly(27).

Only 55% of patients achieve TOF ratios >0.9 within ten minutes of reversal with significant increase in risk (26). Objective neuromuscular monitoring minimizes the incidence of residual paralysis. Moreover, instead of objective monitoring, some anesthesiologists give evaluation together with diffuse clinical signs of reversal when there is no fade-in muscular response to nerve stimulation.(27,28) .

Acceleromyography is the recommended objective method for the detection of the residual block. TOF monitoring was necessary for this study to provide an objective assessment. TOF monitoring was necessary for this study to provide an objective assessment; the TOF ratio of ≥0.9 is ideal for normal vital muscle functions and spontaneousrespiration. So the accepted cut-off value was TOF ratio >0.9. Jones et al. Found that the time to reach 0.90 TOF ratio was 18 times shorter with sugammadex than with neostigmine in a routine reversal of deepNMB.(17)

In comparative studies, it has been shown that sugammadex is more effective than neostigmine in the reversal of NMB when rocuronium or vecuronium was administered. However, they found only cases of severe residual paralysis (TOF ratio <0.7) in combination with a long-acting NMBA (pancuronium) to cause a significant increase in risk. The proportion of residual paralysis found in our investigation is high but in line with previously published data.(22)Apart from the fore mentioned denial of the clinical significance of the problem, other Sugammadex has created a new approach to the rapid reversal of NMB.

Sugammadex is a new pharmacological agent used to reverse the effects of steroidal neuromuscular blockers. If given in

appropriate doses, it may decrease the duration of the effect of rocuronium as of succinylcholine. This property is advantageous in case of difficult intubation or ventilation. Proper sugammadex doses reverse neuromuscular blockade, irrespective of the depth of anesthetic. It does not interfere with the metabolism of acetylcholine. Thus it is not necessary to use anticholinergic drugs concomitantly. Furthermore, it has no proven side effects. It does not have the undesired cholinergic/muscarinic side effects of acetylcholine esterase inhibitors(24). It is recommended that the TOF value should exceed 0.90 in order to avoid.

For choosing the sufficient dose of sugammadex, a dose of 2 mg/kg for reversal of NMB was used in this study, which was supported by a study by Sorgenfrei et al. who compared different doses of sugammadex (0.5, 1, 2, 3, 4mg/kg) with a placebo and found that with every dose of sugammadex the time to reach 0.90 TOF ratio shortened. They also observed that the time to achieve 0.90 TOF ratio was significantly shorter, with sugammadex doses more than or equal to 2 mg/kg.

Makri et al. reported that rebound might be seen in rocuronium effects in the Debaene et al(.25) reported that a TOF measurement for the depth of NMB is essential in deciding the appropriate sugammadex dose. Therefore, administered 2 mg kg−1 sugammadex and measured the depth of NMB with TOF monitoring. Plaud mentioned that in his study, sugammadex has 10 times faster efficiency.

16 mg kg-1 is applied in the case of intense neuromuscular blockade, 4 mg kg-1 for deep neuromuscular blockade, and 2 mgkg-1 for mild neuromuscular blockage. During blockade induced by rocuronium, 2mg kg-1 sugammadex and 50 µg kg-1 neostigmine was compared. Sugammadex had a faster reversal effect than neostigmine(5)

In our study, extubation time was recorded in seconds using a stopwatch. Extubation took 130.37±167.29 seconds after 2 mg kg-1 sugammadex administration. On the other hand, extubation took significantly longer, 269.1±1352.1 seconds, following atropine and neostigmine administration. Khuenl-Brady et al.24 compared neostigmine with sugammadex in a randomizedstudy where it was applied to reverse the medium NMB obtained with rocuronium or vecuronium in adults.112 In the rocuronium group, the duration from sugammadex or neostigmine administration to reach TOF ratio 0.90 was found to be 1.4 min with sugammadex and 17.6 minutes with with neostigmine.

In our study, the mean extubation times were significantly higher in the group RN compared to the group RS. Time to reach the TOF ratio over 0.90 was found to be prolonged in the group RN compared to the group RS. Results in our study were in agreeement with previous studies.We did not conduct a hemodynamic comparison in our study. However, the potential effects of bradycardia, tachycardia, hypotension, and hypertension were observed inneither of the groups.Sugammadex was generally well tolerated in these studies, with no evidenceof residual or recurrence of neuromuscular blocker (NMB) effect. Four patients in the, neostigmine group were reported with adverse events in one study, possibly indicative of inadequate NMB reversal(14) In the same way, Wu et al. obtained considerable data in a multicentre study performed on 230 Chinese subjects (119 received sugammadex, 111 received neostigmine), and 59 Caucasian subjects (29 received sugammadex, 30 received neostigmine). They reported that the time for recovery of the TOF ratio to 0.90 was1.6 (1.5–1.7) minutes with sugammadex and 9.1 (8.0–10.3) minutes with neostigmine in Chinese patients. Corresponding times for Caucasian patients were 1.4 (1.3–1.5) minutes and 6.7 (5.5–8.0) minutes, respectively. Sugammadex 2 mg kg-1 was generally well tolerated with no serious adverse reactions reported. There was no residual NMB or recurrence of NMB effect.(23)

Özgün et al. reported that sugammadex was confidently useable for pediatric patients also.(16) In a randomized, controlled study on adult patients, the reverse effects related to sugammadex were lower than 1% in all cases, and it was advised that this agentwas effective and safe(17). Only one healthy adult patient showed something similar to a slow, allergic reaction, with flushing and tachycardia, following the administration of sugammadex at a dose of 8.4 mg kg-1.

Some other studies reported hypersensitivity and anaphylaxis during sugammadex use (18-21) .We did not make a hemodynamic comparison in our study. However, we did not encounter any adverse effects such as bradycardia, tachycardia, hypotension, and hypertension in patient given sugammadex.

In conclusion, in comparison with neostigmine, sugammadex results in faster curarization and a shorter clinical extubation time following neuromuscular blockade

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References

[1] Griffith HR, Johnson GE: The use of curare in general anesthesia, *Anesthesiology* 3:418-420, 1942.
[2] Wierda JM, de Wit AP, Kuizenga K, Agoston S: Clinical observations on the neuromuscular blocking action of Org 9426, a new steroidal non-depolarizing agent, *Br J Anaesth* 64:521-523, 1990.
[3] Naguib M, Kopman AF, Ensor JE. Neuromuscular monitoringand postoperative residual curarization: a meta-analysis. Br JAnaesth. 2007;98:302---16.
[4] Murphy GS, Szokol JW, Marymont JH, et al. Residual neuromuscular blockade and critical respiratory events in the postoperative care unit. *Anesth Analg* 2008; 107:130–137.
[5] Viby-Mogensen J, Jørgensen BC, Ording H: Residual curarization in the recovery room, Anesthesiology 50:539-541, 1979. 42. Beemer GH, Rozental P: Postoperative neuromuscular function, Anaesth Intensive Care 14:41-45, 1986.
[6] Cope TM, Hunter JM. Selecting neuromuscular blocking drugs for elderly patients. Drugs Aging. 2003;.

[7] Meretoja OA. Neuromuscular block and current treatment strategies for its reversal in children. Paediatr Anaesth. 2010;20:591---604
[8] Naguib M, Kopman AF, Lien CA, et al. A survey of current management of neuromuscular block in the United States and Europe. *Anesth Analg* 2010; 111:110–119
[9] Naguib M. Pharmacology of muscle relaxant and their antago-nist neuromuscular physiology and pharmacology. In: Miller RD,editor. Anaesthesia. 6th ed. Philadelphia: Churchill Livingston;2006. p. 481---572.
[10] Groudine SB, Soto R, Lien C, et al: A randomized, dose-finding, phase II study of the selective relaxant binding drug, sugammadex capable of safely reversing profound rocuronium-induced neuromuscular block, Anesth Analg 104:555-562, 2007.
[11] Bevan JC, Collins L, Fowler C, The primary: Early and late reversal of rocuronium and vecuronium with neostigmine in adults and children, Anesth Analg 89:333-339, 1999
[12] Committee for Medicinal Products for Human Use. European public assessment report (epar) Bridion. http://www.ema.europa.eu/humandocs/Humans/EPAR/bridion/bridion. htm. (accessed 05/07/2010)
[13] Makri I, Papadima A, Lafioniati A, Pappas AB, George K, Nikolaos KE, et al. Sugammadex, a promising reversal drug. A review of clinical trials. Rev Recent Clin Trials. 2011; 6:250–5.
[14] . Bom A, Bradley M, Cameron K, et al: A novel concept of reversing neuromuscular block: chemical encapsulation of rocuronium bromide by a cycledextrin-based synthetic host, *Angew Chem* 41: 266-270, 2002
[15] Shields M, Giovannelli M, Mirakhur RK, et al: Org 25969 (sugammadex), a selective relaxant binding agent for antagonism of prolonged rocuroniuminduced neuromuscular block, Br J Anaesth 96:36-43, 2006.
[16] Lee C, Jahr JS, Candiotti KA, Warriner B, Zornow MH, Naguib M. Reversal of profound neuromuscular block by Sugammadex administered three minutes after rocuronium: a comparison with spontaneous recovery from suxamethonium. *Anesthesiology* 2009; 110: 1020– 5.
[17] Jones RK, Caldwell JE, Brull SJ, Soto RG. Reversal of profound rocuroniuminduced blockade with sugammadex: a randomized comparison with neostigmine. *Anesthesiology* 2008; 109:816–824Murphy GS, Brull SJ. Residual neuromuscular block: Lessons unlearned. Part I: Definitions, incidence and adverse physiologic effects of residual neuromuscular block. Anaesth Analg 2010;111:120- 8.
[18] Craig RG, Hunter JM: Neuromuscular blocking drugs and their antagonists in patients with organ disease, Anaesthesia 64(Suppl 1): 55-65, 2009.
[19] Watts RW, London JA, Van Wijk RM, Lui YL. The influence of unrestricted use of sugammadex on clinical anaesthetic practice in a tertiary teaching hospital. Anaesth Intensive Care 2012;40:333- 9.
[20] Ledowski T, Hillyard S, Kozman A, Johnston F, Gillies E, Greeaway M, *et al*. Unrestricted access to sugammadex: Impact on neuromuscular blocking agent choice, reversal practice and associated healthcare costs. Anaesth Intensive Care 2012;40:340- 3.1–5
[21] 2. Hristovska AM, Duch P, Allingstrup M, Afshari A. The compara- tive efficacy and safety of sugammadex and neostigmine in reversing neuromuscular blockade in adults. A Cochrane systematic review with meta-analysis and trial sequential analysis. Anaesthesia 2018; 73: 631-41.
[22] Plaud B, Meretoja O, Hofmockel R, et al: Reversal of rocuroniuminduced neuromuscular blockade with sugammadex in pediatric and adult surgical patients, Anesthesiology 110:284-294, 2009.
[23] Eikermann M, Zaremba S, Malhotra A, et al: Neostigmine but not sugammadex impairs upper airway dilator muscle activity and breathing, Br J Anaesth 101:344-349, 2008.
[24] Groudine SB, Soto R, Lien C, et al: A randomized, dose-finding, phase II study of the selective relaxant binding drug, sugammadex capable of safely reversing profound rocuronium-induced neuromuscular block, Anesth Analg 104:555-562, 2007.
[25] Debaene B, Plaud B, Dilly MP, Donati F. Residual paralysis in the PACU after a single intubating dose of nondepolarizing muscle relaxant with an intermediate duration of action. Anesthesiology. 2003; 98:1042–8
[26] Drenck NE, Ueda N, Olsen NV, Engbaek J, Jensen E, Skovgaard LT, *et al*. Manual evaluation of residual curarization using double- burst stimulation: A comparison with train of four. Anaesthesiology 1998;70:578- 81.
[27] de Souza CM, Romero FE, Tardelli MA. Assessment of neuromuscular blockade in children at the time of block reversal and the removal of the endotracheal tube. Rev Bras Anestesiol. 2011;61:145–149, 150145, 178183.
[28] Kim KS, Cheong MA, Lee HJ, Lee JM. Tactile assessment for the reversibility of rocuronium-induced neuromuscular blockade during propofol or sevoflurane anesthesia. *Anesth Analg* 2004; 99:1080–1085.