



OUTCOMES OF POSTOPERATIVE RESIDUAL NEUROMUSCULAR BLOCKADE: COMPARISON BETWEEN SUGAMMADEX AND NEOSTIGMINE

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Conflicts of Interest: Nil

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Abstract:

INTRODUCTION: Residual Neuromuscular Blockade is due to incomplete antagonism of Neuromuscular Blockade (NMB) medications. A train of four (TOF) ratios of 0.9 and above is indicative of adequate reversal from NMB. Also it has been shown that, in postoperative period, risk of aspiration would be increased by additional inhibitory effects of residual inhalational anaesthetics, by depressed conscious level on pharyngeal and laryngeal function. Silent aspiration may cause postoperative pneumonia. Especially in elderly patients who are partially paralyzed after anesthesia, pharyngeal secretion is likely to be retained and there may be bacterial overgrowth. The retained secretion may then be aspirated to the laryngeal inlet, predisposing to silent aspiration-induced pneumonia. So assurance of complete reversal of neuromuscular blockade may reduce the incidence of postoperative aspiration-induced pneumonia, together with other respiratory complications.

MATERIAL AND METHODS: Patients included were from the age range of 18 to 65 years who were scheduled to undergo elective surgery during general anesthesia in the supine position. An intravenous cannula was inserted into one forearm vein for routine anesthetic and study drug administration. Another intravenous cannula was inserted into the opposite arm for blood sampling for safety analysis. The anesthetic agents and doses were adjusted to give support and anesthesia was appropriately maintained until recovery of neuromuscular function to a TOF ratio of 0.9. Two drugs were used for reversal of NMB, sugammadex and neostigmine. Blood samples were collected 4 hours after administration of sugammadex or neostigmine, for assessments of blood counts and biochemistry. Urine samples, collected up to 24 h preoperatively were assessed for standard urinalysis.

RESULTS: A total of 100 subjects were included in the study 50 in sugammadex and 50 in neostigmine in each arm. In Sugammadex group there were 50 patients of which 21(42%) were male and 29(58%) were female. As per ASA, in Sugammadex group 5 (10%), 34 (68%) and 1 (22%) were in ASA Physical status I, status II and Status III respectively and in Neostigmine group 4 (8%), 31 (62%) and 15 (30%) were in ASA Physical status I, status II and Status III respectively. There was faster time to recovery in sugammadex group. Most sugammadex patients 34 (68%) recovered within 3 min of administration of drug, and all recovered within 5 min. Most neostigmine patients 39 (78%) recovered 30–60 min after administration, with 22% taking more than one hour to achieve a TOF ratio of 0.9.

CONCLUSION: Profound neuromuscular blockade can be rapidly and reliably reversed by sugammadex in patients and sugammadex also provides a more rapid reversal of neuromuscular blockade than neostigmine.

Introduction

Residual Neuromuscular Blockade is due to incomplete antagonism of Neuromuscular Blockade (NMB) medications. A train of four (TOF) ratios of 0.9 and above is indicative of adequate reversal from NMB. Quantitative assessment of neuromuscular recovery using train of four ratios is considered gold standardⁱ. Most anesthetist cannot perform a quantitative assessment of neuromuscular functionⁱⁱ.

It has been shown that in asymptomatic elderly people, pharyngeal function is often impaired, and residual effect of a neuromuscular-blocking agent after general anesthesia would worsen the impairment. Also it has been shown in healthy young individuals^{iii, iv, v}. Also it has been shown that, in postoperative period, risk of aspiration would be increased by additional inhibitory effects of residual inhalational anesthetics, by depressed conscious level

on pharyngeal and laryngeal function^{vi}. The risk of postoperative aspiration is generally higher, when the trachea is incubated during anesthesia, as tracheal intubation is known to inhibit laryngeal reflexes^{vii}.

Earlier a TOF ratio greater than 0.7 was considered to indicate sufficient recovery from neuromuscular blockade. However, several reports have indicated that this does not guarantee sufficient recovery, and there is an increased risk of postoperative complications like partial paralysis at a TOF ratio of 0.7 or even at 0.8 like such as upper airway obstruction and hypoxia,^{viii, 2}.

Silent aspiration may cause postoperative pneumonia. Especially in elderly patients who are partially paralyzed after anesthesia, pharyngeal secretion is likely to be retained and there may be bacterial overgrowth. The retained secretion may then be aspirated to the laryngeal inlet, predisposing to silent aspiration-induced pneumonia.^{ix}. So assurance of complete reversal of neuromuscular blockade may reduce the incidence of postoperative aspiration-induced pneumonia, together with other respiratory complications.

studies also suggest that the residual effects of neuromuscular blocking agents can prolong postoperative recovery, adversely affect respiratory function, impair airway protective reflexes, and produce unpleasant symptoms of muscle weakness.

MATERIAL AND METHODS

This prospective study was conducted in the Dept. of Anesthesiology at Venkateshwara Institute of Medical Science, Gajraula UP. The study protocol was approved by institutional review and ethical committee.

Patients included were from the age range of 18 to 65 years who were scheduled to undergo elective surgery during general anesthesia in the supine position. Patients excluded were, if they were having difficult airway or were known or suspected to have neuromuscular disorders that might impair neuromuscular blockade; having hepatic and renal dysfunction; , receiving medication at a dose and/or time known to interfere with NMBAs like antibiotics, anticonvulsants, magnesium salts, those in whom the use of neostigmine and/or glycopyrrolate was contraindicated, female pregnant patients, breast-feeding mothers .

Anesthesia: an intravenous cannula was inserted into one forearm vein for routine anesthetic and study

drug administration. Another intravenous cannula was inserted into the opposite arm for blood sampling for safety analysis. The anesthetic agents and doses were adjusted to give support and anesthesia were appropriately maintained until recovery of neuromuscular function to a TOF ratio of 0.9 and until the patient was judged by the anesthesiologist to be ready for tracheal extubation and transfer to the postanesthesia care units.

Neuromuscular function was monitored using the TOF, at the adductor pollicis muscle, starting after induction of anesthesia (before rocuronium administration) and continuing at least until recovery of the TOF ratio to 0.9.

Two drugs were used for reversal of NMB, sugammadex and neostigmine. Blood samples were collected 4hours after administration of sugammadex or neostigmine, for assessments of blood counts and biochemistry. Urine samples, collected up to 24 h preoperatively were assessed for standard urinalysis.

RESULTS

A total of 100 subjects were included in the study 50 in sugammadex and 50 in neostigmine in each arm. Treatment groups were compared with respect to baseline characteristics.

TABLE 1: Base line characteristics of study population

	Sugammadex (n=50)	Neostigmine (n=50)
Male (%)	21(42%)	23(46%)
Female (%)	29(58%)	27(54%)
Age (mean ± SD)	48 ± 16.4	46 ± 19.2
Weight (mean ± SD)KG	57 ± 15.2	56 ± 12.4
ASA Physical status I	5 (10%)	4 (8%)
ASA Physical status II	34 (68%)	31 (62%)
ASA Physical status III	11 (22%)	15 (30%)

ASA: American society of Anaesthesiologist

In Sugammadex group there were 50 patients of which 21(42%) were male and 29(58%) were female. In Neostigmine group there were 50 patients of which 23(46%) were male and 27(54%) were female. Mean age in Sugammadex group was 48 ± 16.4 years and in Neostigmine group was 46 ± 19.2 years. Mean weight in Sugammadex group was 57 ± 15.2 Kg and in Neostigmine group was 56 ± 12.4 Kg. As per ASA, in Sugammadex group 5 (10%), 34 (68%) and 1 (22%) were in ASA Physical status I, status II and Status III respectively and in Neostigmine group 4 (8%), 31

(62%) and 15 (30%) were in ASA Physical status I, status II and Status III respectively.

There was faster time to recovery in sugammadex group. Most sugammadex patients 34 (68%) recovered within 3 min of administration of drug, and all recovered within 5 min. Most neostigmine patients 39 (78%) recovered 30–60 min after administration, with 22% taking more than one hour to achieve a TOF ratio of 0.9. Thus recovery of TOF ratio to 0.7 and 0.8 were significantly ($P < 0.0001$) faster in the sugammadex group than in the neostigmine group. Before discharge from the recovery room, clinical signs of recovery were similar in both the groups. Adverse events were reported in 44(88%) of sugammadex patients and 37 48 (96%) neostigmine patients.

Table 2: Adverse events

Adverse events	Sugammadex group	Neostigmine group
Nausea	14 (28%)	15(30%)
Procedural nausea	10(20%)	6(12%)
Vomiting	4(8%)	8(16%)
flatulence	8(16%)	1(2%)
Dizziness	1(2%)	5(10%)
Muscular weakness	7(14%)	4(8%)
Pharyngeolaryngeal pain	3(6%)	3(6%)

In the sugammadex group nausea was observed in 14 (28%), procedural nausea in 10(20%), vomiting in 4(8%), flatulence in 8(16%), dizziness in 1(2%), muscular weakness in 7(14%) and pharyngeolaryngeal pain in 3(6%). In neostigmine group nausea was observed in 15 (30%), procedural nausea in 6(12%), vomiting in 8(16%), flatulence in 1(2%), dizziness in 5(10%), muscular weakness in 4(8%) and pharyngeolaryngeal pain in 3(6%).

DISCUSSION

There have been several advantages of muscle relaxants such as optimizing surgical conditions, facilitating tracheal intubation, and improving mechanical ventilation. But there are several disadvantages also in use of Neuromuscular Blocking Agents (NMBA) with the most important one being inadequate recovery of neuromuscular function which leads to postoperative pulmonary complications and upper airway muscle weakness. Hence, reversible agents such as acetylcholinesterase inhibitors and sugammadex are used in order to antagonize the effects of nondepolarizing muscle relaxants and also to prevent the complications due to residual curarization^x.

In a study of obese patients undergoing general anesthesia for elective bariatric surgery. they found that mean time to 90% of TOF was 2.7 versus 9.6 minutes and TOF was 109.2% versus 85.5% () in Group sugammadex and Group neostigmine, respectively. This study proves that sugammadex is faster in reversing rocuronium-induced Neuromuscular Blockade compared to neostigmine^{xi}. In a study by Jones et al it has been observed that group received sugammadex of 4 mg/kg and the other group received neostigmine 70 µg/kg along with glycopyrrolate of 14 µg/kg for reversal of NMB. They concluded that sugammadex reversed the rocuronium-induced NMB within 2.9 mins as compared to 50.4 mins with neostigmine and glycopyrrolate^{xii}.

In this study, sugammadex produced a significantly more rapid recovery from neuromuscular blockade. . Reversal of profound neuromuscular blockade was achieved within a geometric mean of 3 min in the sugammadex group *versus* 60 min in the neostigmine. The ability of sugammadex to rapidly reverse blockade is likely to have important clinical implications, and is useful during prolonged surgery in patients who require maintenance of deep neuromuscular blockade throughout the procedure, and would also be beneficial when surgery ends prematurely^{xiii}. The findings of our study are consistent with those from previous studies showing that sugammadex provides fast and safe recovery than neostigmine^{xiv, xv, xvi}. Sugammadex was well tolerated in most of the patients who received this treatment, and its safety profile was at least comparable with that of neostigmine in the current study.

CONCLUSION

Profound neuromuscular blockade can be rapidly and reliably reversed by sugammadex in patients categorized as American Society of Anesthesiologists physical status I–III. Sugammadex also provides a more rapid reversal of neuromuscular blockade than neostigmine. However more randomized control studies are required to conclude the appropriate dose of sugammadex in cases of incomplete reversal following neostigmine treatment.

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