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Effects of Priming with Pancuronium or Rocuronium on Intubation with Rocuronium in Children

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Abstract

Rocuronium is a non-depolarizing neuromuscular blocking agent which has a rapid onset and intermediate duration of action. The goal of this study was to compare the neuromuscular blocking actions of rocuronium with and without a priming dose of pancuronium or rocuronium in children. Thirty patients were randomly allocated into 3 groups. Ten patients received a single dose of 0.6 mg/kg rocuronium (Group I). The others received either 0.015 mg/kg pancuronium (Group II) or 0.06 mg/kg rocuronium (Group III) 3 minutes before an intubating dose of 0.54 mg/kg rocuronium was given. Neuromuscular blockade was measured via accelerographic response to single stimulations (1 Hz) of the ulnar nerve until maximal twitch depression was reached followed by train-of-four (TOF) stimuli (2 Hz) at 15 second intervals for the remainder of recovery. Groups were compared with regard to onset time, duration and recovery indices. The onset time and duration of block did not differ significantly between groups. However, the time to recovery in group II (24.5±9.9 min) was significantly prolonged compared to that in group I (12.7±3.1 min) or group III (12.7±3.9 min). We concluded that the use of rocuronium with a preceding dose of either pancuronium or rocuronium provided no advantage for intubation in children.

Key Words: Neuromuscular relaxants, rocuronium, pancuronium, onset time, priming principle

INTRODUCTION

Succinylcholine is still the standard neuromuscular blocking drug for rapid sequence tracheal intubation. However, its use in children is associated with undesirable side effects. This concern has led investigators to seek on alternative drug for rapid endotracheal intubation. One such agent is rocuronium, a steroidal derivative of vecuronium with a faster onset and intermediate duration of action.[1] However, its onset is still slower than that of succinylcholine.[2] The administration of a subparalyzing dose or priming dose of nondepolarizing relaxants several minutes before the intubating dose is often employed to accelerate the onset of action.[3] This effect has been demonstrated with both a divided dose of the same relaxant or a mixture of relaxants.[4-6]

Therefore, we compared the time course of neuromuscular block after the administration of rocuronium both with and without a priming dose of either pancuronium or rocuronium in children.

MATERIALS AND METHODS

Studies were performed after institutional approval in 30 ASA physical status class I or II patients aged 3−10 years undergoing elective surgical procedures. Patients with hepatic, renal or neuromuscular disease, or those receiving medications known to interfere with neuromuscular transmission were excluded from the study.

The patients were randomly allocated into 3 groups. As a premedication, 0.004 mg/kg of glycopyrrolate was administered by IM injection. Anesthesia was induced with an intravenous dose of 0.001 mg/kg of fentanyl citrate and 5 mg/kg of thiopental sodium followed by the inhalation of 2% enflurane with 50% nitrous oxide and oxygen with a mask. During the study, lactated Ringer's solution was infused (10 ml/kg/hr). Neuromuscular monitoring

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commenced by using an accelerograph (TOF Guard®, Organon, Turnhout, Belgium) to record the electromyographic response of single-twitch contractions (1 Hz) of the adductor pollicis muscle obtained by stimulation of the ulnar nerve with supramaximal stimuli. The control twitch height of a single stimulation was established.

Ten patients received a single dose of 0.6 mg/kg rocuronium (Group I). The others received 0.015 mg/kg pancuronium (Group II) or 0.06 mg/kg rocuronium (Group III) 3 minutes before an intubating dose of 0.54 mg/kg rocuronium was administered. After injection of the intubating dose of rocuronium, we measured lag time (duration of unchanged neuromuscular transmission) and onset time (time from the end of injection until maximal twitch depression or zero twitch height). At this point, a tracheal intubation was accomplished and intubating conditions were assessed using a scale of 1−4 developed by Mehta et al.[6] Continued monitoring of neuromuscular blockade was performed using TOF stimuli (2 Hz) at 15-second intervals.

Anesthesia was maintained with O_2/N_2O at the rate of 2 L/min each and an end-tidal concentration of enflurane at 1.5−2vol%. All patients were monitored using a continuous ECG, oxygen saturation by pulse oximetry (SpO_2), arterial blood pressure, and end-tidal CO_2 tension. After intubation was performed, the duration of action (time interval from the onset to 10%-twitch height recovered) and recovery index (time interval from 25% to 75% twitch height recovered) were recorded in all patients.

The lag time, onset time, duration and recovery index of muscle relaxants were reported as a mean and standard deviation from the mean and analyzed by multiple comparison following ANOVA. For grading the results of intubation conditions, Fisher's exact test was applied. A level of $p<0.05$ was considered significant.

RESULTS

There were no significant differences in age and weight between the groups (Table 1). There were no significant differences in lag time and duration of action between the groups (Table 2 and 3). The onset time was 70.4±11.6 sec in the rocuronium group, 62.8±10.6 sec in the group given pancuronium prior to the administration of rocuronium, and 63.2±8.5 sec in the group primed with rocuronium. These differences were not statistically significant. The recovery index of 24.5±9.9 min in the group pretreated with pancuronium was almost twice as long as those in groups I and III (12.7±3.1 min and 12.7±3.9 min,

Table 1. Patients' Characteristics

	Group		
	I	II	III
Patients' number (M/F)	6/4	7/3	7/3
Age (years)	6.8±2.2	7.1±2.6	6.5±2.1
Weight (kg)	28.2±10.9	24.7±9.6	23.9±7.3

All values are expressed as mean±SD, except patients' number (M, male; F, female). Group I: Single dose of rocuronium only. Group II and III: Rocuronium followed by the preceding dose of pancuronium and rocuronium.

Table 2. Lag Time and Onset Time with the Intubating Dose of Rocuronium

Parameter	Group		
	I	II	III
Lag (seconds)	21.6±2.7	20.0±3.1	20.5±7.6
Onset (seconds)	70.4±11.6	62.8±10.6	63.2±8.5

All values are expressed as mean±SD. Groupings are the same as shown in Table 1. Lag: time interval from the injection of rocuronium to the beginning of twitch depression. Onset: time interval from the injection of rocuronium to the maximal twitch depression or 0-twitch height.

Table 3. Duration and Recovery Index (RI)

Parameter	Group		
	I	II	III
Duration (minutes)	24.2±7.6	25.7±7.4	21.7±6.0
RI (minutes)	12.7±3.1	24.5±9.9*	12.7±3.9

All values are expressed as mean±SD. Groupings are the same as shown in Table 1. Duration: time interval from onset to 10%-twitch height recovered after rocuronium, RI: time interval from 25% to 75% twitch height recovered.
*: $p<0.05$ vs Group I & III.

Table 4. Grading* of Intubation

Grade	Group		
	I	II	III
1	8	10	7
2	2	0	3
3	0	0	0
4	0	0	0

Groupings are the same as shown in Table 1.
Variables are given in the number of patients.
*Originated from Mehta et al. (1985). Grades 1, 2, 3, and 4: easy passage tube without coughing, passage of tube with slight coughing or bucking or both, passage of tube with moderate coughing or bucking or both, and not possible, respectively.

respectively). No difference in intubating conditions was statistically significant among the groups (Table 4).

DISCUSSION

The goal of this study was to examine the onset time of rocuronium both with and without a preceding dose of rocuronium or pancuronium for rapid endotracheal intubation in children compared with rocuronium alone. The results of the present study suggest that the use of rocuronium preceded by a priming dose of either pancuronium or rocuronium did not significantly shorten the onset. However, the recovery index was significantly prolonged in the pancuronium-pretreatment group.

Rocuronium is a non-depolarizing muscle relaxant with a rapid onset, but slower than that of succinylcholine. The priming principle has been shown to accelerate the onset of neuromuscular blockade for various nondepolarizing relaxants. In this study, the onset of rocuronium was not significantly shortened by use of the priming principle.

It has been reported that priming with pancuronium accelerated the onset time of d-tubocurarine significantly in children,[7] and that the administration of 0.015 mg/kg of pancuronium 3 minutes before the administration of mivacurium significantly hastened the onset of neuromuscular blockade compared to saline.[5] Mehta et al. demonstrated that the onset of neuromuscular blockade is faster when the administration of a nondepolarizing neuromuscular blocking agent is preceded by a smaller dose of the same drug or another nondepolarizing neuromuscular blocking drug.[6] One suggested mechanism of action for this phenomenon is that a small (usually subparalyzing) dose of nondepolarizing neuromuscular blocking drug may partially occupy the postjunctional receptor and/or inhibit presynaptic release of acetylcholine, thus allowing for the more rapid and profound effect of a subsequent dose.[8] The differing abilities of neuromuscular blocking drugs to inhibit neuromuscular transmission by blocking the ionophores on postjunctional membranes may play some role in shortening the onset of neuromuscular blockade when combinations of these drugs are used.[9] It has been suggested that the combination of rocuronium and mivacurium could possibly be considered as an acceptable alternative to succinylcholine when rapid sequence induction of anesthesia is indicated in children because it consistantly provides excellent uniform intubating conditions and complete neuromuscular block within 60 seconds.[10] Increasing the dose of rocuronium accelerates the onset of neuromuscular block and prolongs recovery time.[2,11] In this study, the total dose of neuromuscular blocking agent was $2 \times ED_{95}$ in the study patients. Patients in groups I, II, and III received rocuronium $2 \times ED_{95}$, pancuronium $0.2 \times ED_{95}$ and rocuronium $1.8 \times ED_{95}$, and rocuronium $0.2 \times ED_{95}$ and rocuronium $1.8 \times ED_{95}$, respectively.

However, Foldes et al. reported that priming did not shorten the onset time of $2 \times ED_{95}$ of rocuronium.[12] It has been shown that the onset of neuromuscular blockade in pediatric patients could be accelerated by administering pancuronium in divided doses, but that this difference was so small that such a technique did not appear to convey any clinical advantages. The decrease in onset time using the priming technique in pediatric patients was less than that in adults. In part, this was a reflection of the shorter onset time in children, so that the differences in absolute terms were less.[13] Since the onset time of rocuronium is rapid, any shortening of the onset of action using priming is also likely to be small, as it was in our study.

Pancuronium was chosen as a priming agent because previous studies found that a shorter time to neuromuscular block occurred after "priming" with a drug known to have the ability to potentiate the effect of the second drug.[5,7] Pancuronium, with a presynaptic as well as postsynaptic effect, possesses

this quality.[14] However this study showed no apparent acceleration of onset in Group II. That may be due to a short circulation time or rapid onset of rocuronium.

In this study, recovery was delayed significantly in children primed with pancuronium compared to children receiving either a single dose of rocuronium or divided doses of rocuronium. Mixtures of 2 different relaxants may potentiate each other due to differences in the pre- and postsynaptic activity among relaxants, or because of the different affinities of the relaxants for the 2 subunits of the acetylcholine receptor.[8,15] This synergism in addition to its long elimination half life may explain the delayed recovery observed in the group pretreated with pancuronium.

Agoston et al. and Gergis et al. have observed that good intubating conditions are present when 40–60% and 70% twitch inhibition of the addictor pollicis muscle is obtained, respectively.[16,17] In this study, 95% or greater twitch height inhibition of the adductor pollicis at intubation was seen in all patients and it provided good to excellent intubating conditions in all patients.

In summary, rocuronium provided good intubating conditions in all children in our study. Priming of an intubating dose of rocuronium with pancuronium or rocuronium slightly decreased the onset of neuromuscular block, but this difference was not significant. Prior administration of a small dose of pancuronium significantly increased the spontaneous recovery induced by rocuronium. In conclusion, a priming dose of rocuronium or pancuronium provided no advantages compared to a single dose of rocuronium in children.

REFERENCES

1. Wierda JMKH, de Wit APM, Kuizenga K, Agoston S. Clinical observations on the neuromuscular blocking action of ORG 9426, a new steroidal non-depolarizing agent. Br J Anaesth 1990;64:521-3.
2. Magorian T, Flannery KB, MIller RD. Comparison of rocuronium, succinylcholine, and vecuronium for rapid sequence induction of anesthesia in adult patients. Anesthesiology 1993;79:913-8.
3. Savarese JJ, Miller RD, Lien CA, Caldwell JE. In: Miller RD, editor. Anesthesia. 4th ed. New York: Churchill Livingstone Inc.; 1994. p.436.
4. Schwarz S, Ilias W, Lackner F, Mayrhofer O, Foldes FF. Rapid tracheal intubation with vecuronium: The priming principle. Anesthesiology 1985;62:388-91.
5. Brandom BW, Meretoja OA, Taivainen T, Wirtavuori K. Accelerated onset and delayed recovery of neuromuscular block induced by mivacurium preceded by pancuronium in children. Anesth Analg 1993;76:998-1003.
6. Mehta MP, Choi WW, Gergis SD, Sokoll MD, Adolphson AJ. Facilitation of rapid endotracheal intubations with divided doses of nondepolarizing neuromuscular blocking drugs. Anesthesiology 1985;62:392-5.
7. Smith CE, Baxter M, Bevan JC, Donati F, Bevan DR. Accelerated onset and delayed recovery of d-tubocurarine blockade with pancuronium in infants and children. Can J Anaesth 1987;34:555-9.
8. Bowmann WC. Prejunctional and postjunctuinal cholinoceptors at the neuromuscular junction. Anesth Analg 1980; 59:935-43.
9. Dreyer F. Acetylcholine receptor. Br J Anaesth 1982;54: 115-30.
10. Naguib M, Samarkandi AH, Ammar A, Turkistani A. Comparison of suxamethonium and different combinations of rocuronium and mivacurium for rapid tracheal intubation in children. Br J Anaesth 1997;79:450-5.
11. Woolf RL, Crawford MW, Choo SM. Dose-response of rocuronium bromide in children anesthetized with propofol: a comparison with succinylcholine. Anesthesiology 1997;87:1368-72.
12. Foldes FF, Nagashima H, Nguyen HD, Schiller WS, Mason MM, Ohta Y. The neuromuscular effects of ORG 9426 in patients receiving balanced anesthesia. Anesthesiology 1991;75:191-6.
13. Bevan JC, Donati F, Bevan DR. Attempted acceleration of the onset of action of pancuronium. Br J Anaesth 1985;57:1204-8.
14. Robbins R, Donati F, Bevan DR, Bevan JC. Differential effects of myoneural blocking drugs on neuromuscular transmission in infants. Br J Anaesth 1984;56:1095-9.
15. Lebowitz PW, Ramsey FM, Savarese JJ, Ali HH. Potentiation of neuromuscular blockade in man produced by combinations of pancuronium and metocurine or pancuronium and d-tubocurarine. Anesth Analg 1980;59: 604-9.
16. Agoston S, Salt P, Newton D, Bencini A, Boomsma P, Erdmann W. The neuromuscular blocking action of ORG NC45, a new pancuronium derivative, in anaesthetized patients. Br J Anaesth 1980;52:53S-9S.
17. Gergis SD, Sokoll MD, Mehta M, Kemmotsu O, Rudd GD. Intubation conditions after atracurium and suxamethonium. Br J Anaesth 1983;55:83S-6S.