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Rapid Tracheal Intubation with Vecuronium: The Priming Principle

Sylvia Schwarz, M.D., Wilfred Ilias, M.D.,* Franz Lackner, M.D.,†*
Otto Mayrhofer, M.D.,‡ Francis F. Foldes, M.D.§

Following the administration of a single 0.1 mg/kg dose of vecuronium bromide, satisfactory conditions for tracheal intubation developed in 156 ± 12 s (mean ± SEM), and the clinical duration of the initial dose was 36 ± 2 min. When the initial dose of vecuronium was administered in two increments, a 0.015 mg/kg "priming" dose, followed 6 min later by a 0.050 mg/kg "intubating" dose, intubation time decreased to 61 ± 3 s and clinical duration to 21 ± 1 min. The priming dose that had no unpleasant effect on premedicated, awake patients could be administered 3–4 min before, and the intubating dose 2 to 3 min after induction of anesthesia. With the described technique, comparable intubating conditions could be obtained just as rapidly with vecuronium as with succinylcholine chloride, without subjecting the patients to the side effects of and the complications occasionally encountered with succinylcholine. An added advantage of the use of a priming dose is that it will reveal undiagnosed, pathologic, or idiopathic increase of sensitivity to nondepolarizing muscle relaxants. (Key words: Induction: anesthesia, rapid sequence. Neuromuscular relaxants: succinylcholine; vecuronium.)

FAST ONSET of action, permitting early tracheal intubation, is one of the desirable properties of neuromuscular (NM) blocking agents (muscle relaxants, MR). With the current method of administration of MR, this can be achieved with succinylcholine chloride (SCh). SCh, however, has numerous side effects and occasionally may cause serious complications.[1] With reasonable doses of nondepolarizing MR, conditions suitable for tracheal intubation cannot be achieved in less than 2–3 min, and the onset time required for the development of their maximal effect is 5–6 min. This applies equally to the long-acting MR, such as pancuronium bromide[2] and to the new, relatively short-acting nondepolarizing MR, vecuronium bromide[3] and atracurium besylate.[3] Furthermore, with the exception of vecuronium, "intubating" doses of muscle relaxants may have cardiovascular and other unwanted side effects.[1]

Exploring various possibilities for shortening the time interval between the injection of the "intubating" dose of a nondepolarizing MR and the development of muscular relaxation, permitting atraumatic intubation, it occurred that this may be accomplished by the injection of MR in divided doses.[4] The rationale of the divided dose technique of administration of MR for facilitation of rapid tracheal intubation is based on the following: 1) the high margin of safety of NM transmission that allows 70 to 75% occupancy of the cholinergic receptors without any significant effect of NM activity[5]; 2) the observation that doses of MR that moderately decreased grip strength, indicating greater than 70% receptor occupancy, caused no unpleasant symptoms in conscious volunteers[6]; and 3) the onset time of marginally effective doses of MR was 5–8 min.[6] It was assumed that administration of a second, larger dose of a MR, at the time of development of the maximal effect of the "priming" dose, rapidly would increase receptor occupancy to the 90–92% level required for profound NM block.[5] It subsequently was determined by trial and error that about 15–20% of the customary "intubating" doses of vecuronium, atracurium, or alcuronium chloride, followed by 50–60% of the usual intubating dose administered after induction of anesthesia and 6–7 min after the priming dose, produced satisfactory muscular relaxation for tracheal intubation in 40–90 s. Encouraged by the results obtained, with the divided dose method of administration of MR in these pilot studies, it was decided to investigate the effect of different combinations of priming and intubating doses on the onset time (time from the start of injection to the development of maximal effect) and clinical duration (time from start of injection to the return of the twitch to 25% of control) of vecuronium.

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* Assistant Anesthesiologist, University of Vienna Medical School.
† Professor of Anesthesiology, University of Vienna Medical School.
‡ Professor of Anesthesiology and Chairman, Department of Anesthesiology, University of Vienna Medical School.
§ Consultant, Department of Anesthesiology, Montefiore Medical Center.

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Address reprint requests to Dr. Foldes: Montefiore Medical Center, 111 East 210th Street, Bronx, New York 10467.

Methods and Materials

Observations on the NM effects of vecuronium administered in divided doses were made in the Department of Anesthesiology of the University of Vienna Medical School. The investigation was approved by the Ethics Committee of the Medical School, and all patients included signed informed consents.

ASA classification I and II patients of either sex whose ages ranged from 16 to 70 yr and weighed 50 to 91 kg were premedicated with 1 mg/kg intramuscular meperidine hydrochloride and 0.07 mg/kg intravenous diazepam. Balanced anesthesia was induced with 0.1 mg/kg droperidol, 1 μg/kg fentanyl citrate, and 3 mg/kg thiopental sodium. If the lid reflex was not abolished by the initial dose, 50 mg increments of thiopental were injected 15 s apart until the lid reflex disappeared. Anesthesia was maintained with N_2O, 4 l/min in O_2 2 l/min and 25 to 100 μg increments of fentanyl.

After induction of anesthesia, 300–400 g, pretension was applied to the thumb. The ulnar nerve at the wrist was stimulated through surface electrodes by supramaximal impulses of 0.2 ms duration at 0.1 Hz. The indirectly elicited twitch tension of the adductor pollicis muscle was quantitated by force displacement transducers and recorded continuously. When the twitch tension became stable, the priming dose of vecuronium was administered: 10 patients (Group 1) and seven others (Group 2) received 0.015 mg/kg; 12 others (Group 3) received 0.02 mg/kg. Trains-of-four (T4), 2-Hz stimuli[7] were applied immediately before and at 5 min after the injection of the priming dose. To ensure satisfactory depth of anesthesia for intubation, at 5 min 1 μg/kg fentanyl was injected. At 6 min patients in Group 1 received 0.05 mg/kg and those in Groups 2 and 3 0.06 mg/kg vecuronium injected quickly into a rapidly flowing intravenous infusion. When the twitch tension decreased to 15–25% of control, the trachea was intubated.¶ Intubating conditions were scored as follows: excellent = 3 (jaw relaxed, vocal cords apart and immobile, no diaphragmatic movement); good = 2 (conditions as in 3, except that there is some diaphragmatic movement); poor = 1 (jaw relaxed, cords moving; bucking); inadequate = 0 (jaw poorly relaxed, cords closed, coughing). The intubation time (time between the injection of the intubating dose and intubation) as well as the onset time and clinical duration were noted.

To simulate clinical conditions, 10 other patients (Group 4), premedicated and anesthetized as the others, received a 0.015 mg/kg priming dose of vecuronium after premedication but before induction of anesthesia.

¶ Previous experience indicated that at this time relaxation for tracheal intubation is satisfactory.[8]

TABLE 1. The Neuromuscular Effect of Priming Doses of Vecuronium

Priming Dose (mg/kg)	5 Min after Priming Dose	
	Twitch Tension (%)	T4/T1 Ratio
0.015 (17)*	84.7 ± 2.1†	0.77 ± 0.03
0.020 (12)	87.5 ± 5.0	0.63 ± 0.05‡

* Number of observations.
† Mean ± SEM.
‡ $P < 0.05$; Student's t test.

Induction of anesthesia was so timed that the time interval between the priming and the 0.05 mg/kg intubating dose was 6 min. These patients were arbitrarily intubated 80 s after injection of the intubating dose. Assessment of NM activity, based on visual observation of the response to T4 stimulation of the ulnar nerve, was started only after intubation. Therefore, onset time could not be determined in these patients. The clinical duration of the intubating dose was assumed to be equal to the time interval between injection of the intubating dose and the first visible response to the second of the T4 stimuli.

For sake of comparison intubation time, onset time and clinical duration also were determined in two additional groups of patients of similar physical status and sex, age, and weight distribution. Premedication and anesthesia was also similar to that used in the first three groups. Fifteen patients (Group 5) received a single 0.1 mg/kg dose of vecuronium, and 29 others (Group 6) 0.6 mg/kg SCh for the facilitation of tracheal intubation. The observations on Groups 5 and 6 were made in the Department of Anesthesiology of the Montefiore Medical Center, Bronx, New York. These studies were approved by the Institutional Review Board, and patients signed informed consent forms.

Statistical significance of the differences of the various parameters observed in different groups were determined with analysis of variance and Dunn's t test.

Results

The 0.015 mg/kg and the 0.02 mg/kg priming doses of vecuronium caused similar decrease of the twitch (table 1). The T4/T1 ratio, however, was lower ($P < 0.05$; Student's t test) after the 0.02 mg/kg than after the 0.015 mg/kg priming dose.

The size of the priming dose or intubating dose had no influence on intubation time, onset time, and intubation score (table 2). Clinical duration, however, was somewhat longer ($P < 0.002$) in Group 3 (priming dose 0.02 mg/kg, intubating dose 0.06 mg/kg) than in Group 1 (priming dose 0.015 mg/kg, intubating dose 0.05 mg/kg).

TABLE 2. Intubation Time, Intubating Conditions, Onset Time, and Clinical Duration

Group	Number of Patients	Dose (mg/kg) of Vecuronium		Intubation		Onset Time (s)	Clinical Duration (min)
		Priming	Intubating	Time (s)	Score*		
1	10	0.015	0.05	61 ± 3†	3 in 9 2 in 1	98 ± 11	18 ± 1
2	7	0.015	0.06	69 ± 7	3 in 6 2 in 2	125 ± 18	23 ± 3
3	12	0.020	0.06	55 ± 3	3 in 10 2 in 2	84 ± 5	27 ± 3
4	10	0.020	0.05	80‡	3 in 8 2 in 2	—	25 ± 2
5	15	—	0.1	156 ± 12§	3 in 9 2 in 6	354 ± 60§	36 ± 2§
6	29	—	SCh 0.6 mg/kg	66 ± 6	3 in 20 2 in 9	96 ± 6	6.3 ± 0.1§

* Excellent = 3; good = 2. For definitions see "Methods."
† Mean ± SEM.
‡ Intubation performed arbitrarily at 80 s.
§ Indicates difference from other values in same vertical column at the $P < 0.001$ level.

The 10 patients of Group 4, who received 0.015 mg/kg vecuronium while awake, experienced no discomfort during the 3–4 min that elapsed until the administration of thiopental. Following the administration of the 0.05 mg/kg intubating dose of vecuronium, they arbitrarily were intubated at 80 s. Intubation score and clinical duration in this group were similar to those observed in Groups 1, 2, and 3.

In patients who had no priming dose and received a single 0.1 mg/kg intubating dose of vecuronium (Group 5), the intubation score was similar to those observed in Groups 1, 2, and 3. Intubation time, onset time, and clinical duration, however, were longer ($P < 0.001$) than in Groups 1, 2, and 3.

Intubation time, intubation score, and onset time in patients intubated after a single 0.6 mg/kg dose of succinylcholine (Group 6) were very similar to those observed in Groups 1, 2, and 3. However, the clinical duration in this group was much shorter ($P < 0.001$) than in the vecuronium groups.

Discussion

The divided-dose method of administration of the initial dose compensates for the relatively slow onset of action of vecuronium. It provides excellent conditions for tracheal intubation just as rapidly as SCh. In contrast to SCh, however, vecuronium is free of side effects, and therefore there are no known contraindications to its use.

Intubation time, intubation score, and onset time were about the same with 0.015/0.05, 0.015/0.06, or 0.02/0.06 mg/kg combinations of priming and intubating doses. In patients hypersensitive to nondepolarizing MR, the likelihood of ptosis, double vision, and swallowing difficulty may be greater after the larger than after the smaller priming dose. Therefore, in clinical practice the smaller priming dose is preferable. Such unexpected hypersensitivity to nondepolarizing MR can be encountered not only in undiagnosed myasthenia gravis,[9] carcinomatous neuropathy,[10] and various other NM disorders[11] but also in a small percentage of normal individuals, without any apparent reason.[12]

Larger than the suggested intubating doses may be used, however, when it is especially important to decrease the time interval between induction of anesthesia and tracheal intubation and the clinical duration of the intubating dose is less important. The need for this arises in patients with full stomachs, who for some reason cannot be intubated wake, and in the presence of penetrating eye wounds. SCh is contraindicated in such patients. In addition to the facilitation of rapid intubation, there are two other advantages to the divided-dose method of administration of vecuronium. The first of these is that, since the sum of the priming and intubating doses is smaller than the conventional intubating dose, the clinical duration of the first dose is reduced by about 25%. This may be desirable in short surgical procedures. The second advantage is that the exaggerated reaction of a patient to the priming dose will alert the anesthesiologist to the presence of hypersensitivity to nondepolarizing MR.

At first sight it may appear that the divided-dose technique may prolong unduly induction time. In reality, however, this is not the case. The priming dose, similar to the small "precurarizing" doses of nondepolarizing MR, frequently used in conjunction with SCh, can be administered to awake patients as soon as an intravenous infusion has been started. Preparation for and induction of anesthesia take several minutes. Therefore, induction can be planned without any time loss in a way that the patient will be ready for the intubating dose of vecuronium 5–7 min after the priming dose.

As already indicated, patients who are unusually sensitive to nondepolarizing MR may have double vision or swallowing difficulties 2–3 min after the injection of the priming dose. Because of the decreased effect of nondepolarizing MR on the diaphragm,[6,13] it is unlikely that the respiratory tidal volume will be affected greatly in these patients. Despite this, if a patient feels uncomfortable after injection of the priming dose, anesthesia should be induced immediately with thiopental or metohexital sodium and the patient ventilated with oxygen. In these patients, the size of the intubating dose of vecuronium should be reduced, in proportion to the intensity of the NM effect of the priming dose, to 0.02–0.04 mg/kg.

While this study has been in progress, it came to our attention that Gergis *et al.*[14] also recommended a divided-dose method for the facilitation of rapid tracheal intubation with atracurium. The 0.08 mg/kg priming dose recommended by them was also about 15% of the usual intubating dose. They, however, only allowed 3 min to elapse between the administration of the priming and the intubating doses. Probably because of this, despite the larger 0.42 mg/kg intubating dose (about 85% of the customary intubating dose of atracurium), satisfactory relaxation for tracheal intubation only developed in 90–120 s. Their prediction that the administration of a priming dose will facilitate rapid tracheal intubation, not only with atracurium but also with other nondepolarizing MR, has been confirmed for vecuronium in this study.

References

1. Walts LF: Complications of muscle relaxants, Muscle Relaxants. Edited by Katz R. New York, Elsevier Publishing, 1975, pp 209–244
2. Nagashima H, Stoll M, Nguyen H, Duncalf D, Foldes FF: Surgical relaxation with metocurine–pancuronium combinations. Anesth Analg 63:254, 1984
3. Foldes FF, Nagashima H, Boros M, Tassonyi E, Fitzal S, Agoston S: Muscular relaxation with atracurium, vecuronium and Duador under balanced anesthesia. Br J Anaesth 55:97S–103S, 1983
4. Foldes FF: Tracheal intubation with nondepolarizing muscle relaxants: The priming principle (Letter to the editor). Br J Anaesth 1984, In press
5. Paton WDM, Waud DR: The margin of safety of neuromuscular transmission. J Physiol (Lond) 191:59–90, 1967
6. Foldes FF, Monte AP, Brunn HM, Wolfson B: Studies with muscle relaxants in unanesthetized subjects. ANESTHESIOLOGY 22:230–236, 1961
7. Ali HH, Kitz RJ: Evaluation of recovery from nondepolarizing neuromuscular block, using a digital neuromuscular transmission analyzer. Preliminary report. Anesth Analg 52:740–745, 1973
8. Duncalf D, Nagashima H, Hollinger I, Badola RP, Kaplan R, Foldes FF: Relaxation with Org-NC45 during enflurane anesthesia (abstract). ANESTHESIOLOGY 55:A203, 1981
9. Bennett AE, Cash PT: Myasthenia gravis and curare sensitivity. Diseases of Nervous System 4:299–301, 1943
10. Eaton LM, Lambert EH: Electromyography and electric stimulation of nerves in diseases of motor unit: observations on the myasthenic syndrome associated with malignant tumors. JAMA 163:1117–1124, 1957
11. Cohen EN: Patients with altered sensitivity, Muscle relaxants. Edited by Foldes FF. Philadelphia, FA Davis, 1966, pp 75–93
12. Pelikan EW, Tether JE, Unna KR: Sensitivity of myasthenia gravis patients to d-tubocurarine and decamethonium. Neurology 3:284–296, 1953
13. Tran DQ, Amaki Y, Ohta Y, Nagashima H, Duncalf D, Foldes FF: Simultaneous in vivo measurement of NM block on three muscles (abstract). ANESTHESIOLOGY 57:A276, 1982
14. Gergis SE, Sokoll MD, Mehta M, Kemmotsu O, Rudd GD: Intubation conditions after atracurium and suxamethonium. Br J Anaesth 55:83S–86S, 1983