Rapid-SequenCe Orotracheal Intubation: A Comparison of Three Techniques

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The authors compared tracheal intubating conditions using three techniques for rapid-sequence orotracheal intubation. Sixty patients were randomly assigned to one of three groups: priming with vecuronium (0.01 mg/kg priming dose, 4-min priming interval, 0.14 mg/kg intubating dose along with thiopental 4–6 mg iv; timing with vecuronium (0.15 mg/kg intubating dose given before thiopental and timed to weakness of hand grip) and succinylcholine (1.5 mg/kg). Blinded intubators graded intubating conditions 60 s after the induction of anesthesia with thiopental. Intubation scores in the succinylcholine group were significantly better than in the priming group (P = 0.009). Intubation scores of the succinylcholine and the timing groups were not significantly different. Use of the timing principle for rapid-sequence orotracheal intubation is a reliable alternative in cases where succinylcholine is contraindicated. Key words: Intubation; rapid-sequence. Neuromuscular relaxants: succinylcholine; vecuronium. Pharmacodynamics: "The Timing Principle;" "The Priming Principle;"

Rapid-Sequence Induction and orotracheal intubation is an established technique in patients considered to be at risk for aspiration of gastric contents. To date, the most reliable muscle relaxant for this purpose is succinylcholine. Succinylcholine is controversial; it has a number of undesirable side effects and it may be contraindicated in certain cases.1 The potential problems associated with succinylcholine have prompted the search for alternative methods of using nondepolarizing muscle relaxants. The priming principle2-4 uses divided doses of muscle relaxant and is one such alternative to succinylcholine. However, this technique has limitations. The incidence of coughing and bucking may approach 20–40%.5 This limits its application in patients with open-eye injuries or increased intracranial pressure.

Recently, the timing principle6 using vecuronium bromide was studied as an alternative to the priming principle. This technique yielded excellent intubating conditions 60 s after induction of anesthesia with thiopental. The timing principle uses a single bolus dose of nondepolarizing muscle relaxant, followed by administration of an induction agent that is timed to the onset of clinical weakness. The current study was undertaken to evaluate intubating conditions in the use of three techniques of rapid orotracheal intubation: the timing principle, the priming principle, and succinylcholine.

Materials and Methods

This study was approved by our institutional review board and written informed consent was obtained from each patient. Sixty ASA physical status 1 and 2 patients aged 18–76 yr (mean 33 ± 4) undergoing elective surgery were selected for this randomized single-blinded study. Exclusion criteria included pregnancy, age less than 18 yr, an increased risk of aspiration (gastroesophageal reflux, morbid obesity), asthma, or a potentially difficult airway or history of difficult tracheal intubation. Patients were randomly assigned by sealed envelope to one of three groups, each composed of 20 patients: timing with vecuronium, priming with vecuronium, or succinylcholine (control). The flow diagram (fig. 1) summarizes the study design.

Preatheastic medication consisted of ranitidine 150 mg by mouth the evening before surgery, and ranitidine 150 mg by mouth with metoclopramide 10 mg the morning of surgery. After arrival in the operating suite, an 18-G or larger peripheral intravenous cannula was inserted. Routine monitoring included ECG, automated blood pressure cuff (Dinamap®), pulse oximetry, precordial stethoscope, and mass spectrometry. Transcutaneous nerve stimulator electrodes were placed over the ulnar nerve at the elbow. After loss of consciousness, neuromuscular blockade was visually estimated with a train-of-four every 10 s with a Digi-stim II® nerve stimulator.

All patients inspired 100% oxygen by mask for 2–3 min prior to the induction sequence, and midazolam 0.03–0.06 mg/kg was administered intravenously.

Timing Group

Patients were asked to firmly squeeze the investigator's fingers to permit assessment of baseline hand-grip strength. Prior to the administration of vecuronium, all patients were told that they would experience weakness but to continue with their strongest attempts at hand grip.

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They also were told they may experience diplopia, or respiratory weakness. Vecuronium 0.15 mg/kg was administered intravenously, and every 10 s each patient was asked to demonstrate a maximal hand grip. Respiratory status was monitored by chest movement, breath sounds, movement of the reservoir bag, and capnography trace on the mass spectrometer. At the onset of clinical weakness, as judged by weakness of hand grip or decreased respiratory effort, patients were asked to cough. The ability to cough was a gross assessment of the patient’s ability to protect their airway. The time of onset of weakness was recorded. Thiopental 4–6 mg/kg was promptly given as the induction agent. Sixty seconds after the administration of thiopental the trachea of each patient was intubated.

**PRIMING GROUP**

After administration of midazolam, all patients were given 0.01 mg/kg vecuronium. Patients were observed for 4 min while breathing 100% oxygen. They were told that they may experience weakness after the administration of the priming dose. Respiratory efforts were monitored in the same manner as were patients in the timing group. Hand grip was not assessed. All patients then were asked to cough and were given 0.14 mg/kg vecuronium as an intravenous bolus followed immediately by 4–6 mg/kg thiopental. Sixty seconds after thiopental the trachea of each patient was intubated.

**SUCCINYLCHOLINE GROUP (CONTROL)**

After administration of midazolam, the patients were given 3 mg D-tubocurare intravenously and observed for 4 min while breathing 100% oxygen. Respiratory efforts were monitored in the same manner as the other groups. Patients were asked to cough and given 1.5 mg/kg succinylcholine followed immediately by 4–6 mg/kg thiopental intravenously. Sixty seconds after thiopental, the trachea of each patient was intubated.

All tracheal intubations in the study were performed by staff anesthesiologists or certified registered nurse anesthetists (CRNAs) with at least 5 yr of clinical experience. These individuals were blinded to the induction sequence by remaining outside the operating room and entering 20 s prior to intubation. The delayed entry into the operating room was to avoid the observation of any succinylcholine-induced fasciculations by the intubators. The adequacy of intubating conditions was assessed by the blinded individual based on an established scale (Table 1). All induction agents were administered by a non-blinded investigator (S.S.) who also recorded bucking or any movement in response to endotracheal intubation. However, the final grade was determined by the individual performing the endotracheal intubation.

Visual estimate of the train-of-four measurements was made at the time of tracheal intubation. Blood pressure and heart rate were recorded just prior to induction and immediately after tracheal intubation. Time to return of the first twitch in the train-of-four also was determined for each patient. This time was measured from the administration of the intubating dose of muscle relaxant to the return of the first twitch in the train-of-four after complete twitch ablation. Maintenance anesthesia in all groups consisted of a balanced anesthetic of nitrous oxide,

**TABLE 1. Grading of Intubating Conditions**

<table>
<thead>
<tr>
<th>Score</th>
<th>Timing (n = 20)</th>
<th>Priming (n = 20)</th>
<th>Succinylcholine (n = 20)</th>
</tr>
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<tbody>
<tr>
<td>3</td>
<td>16</td>
<td>12</td>
<td>19</td>
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<td>2</td>
<td>4</td>
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Intubation scores: 3 = Excellent (jaw relaxed, cords abducted, no movement). 2 = Good (same as 3 except slight cough or movement). 1 = Poor (jaw poorly relaxed, cords moving, bucking). 0 = Unable to intubate.
fentanyl, and isoflurane. All patients were interviewed on the day after surgery and specifically questioned about recall of perioperative events (i.e., weakness prior to induction) and overall satisfaction.

Intubation scores were analyzed with a Kruskal-Wallis analysis of variance for nonparametric data, and between-group comparisons were analyzed with a Mann-Whitney $U$ test, corrected for ties. Demographic data were analyzed with one-way analysis of variance. Time to return of a single twitch was compared between timing and priming groups with an unpaired Student’s $t$ test. A $P$ value $< 0.05$ was considered statistically significant.

**Results**

All results in tables are mean ± SEM unless otherwise indicated.

Demographic data were similar for all three groups (Table 2). Thiopental doses were not different between groups (Table 2). Intubation scores, train-of-four estimates at the time of intubation, and time for return of first twitch are summarized in Tables 1, 3, and 4.

Intubation score results are summarized in Table 1. All patients in the study received intubation scores of 2 or 3, indicating good or excellent intubating conditions. Succinylcholine yielded excellent conditions in 19 patients. Intubation scores in the succinylcholine group were significantly higher than those in the priming group ($P = 0.009$). Intubation scores in the timing group were not significantly different when compared with those receiving succinylcholine ($P = 0.157$). In the timing group, the mean onset to clinical weakness was $56 ± 3$ s. Time to return of first twitch in the train-of-four was not significantly different between timing and priming groups ($P = 0.054$; Table 4).

Patients with intubation scores of 2 demonstrated coughing or bucking after tracheal intubation. This usually was observed as slight abdominal movement. The intensity of movement was greater in some patients than in others. Since the degree of abdominal movement was not incorporated into the intubation score, any movement observed was scored less than 3. In the succinylcholine group one patient exhibited very slight abdominal movement after tracheal intubation. In the timing group, three patients who scored 2 exhibited very slight abdominal movement.

In the priming group, all patients who scored 2 were observed by the intubator to have bucking or coughing as evidenced by gross motion of the trunk or abdomen. The degree of motion was noted to be greater than that of the timing or succinylcholine groups. One priming patient experienced significant weakness and respiratory difficulty approximately 2.5 min after the priming dose, and anesthesia was induced immediately. The subsequent intubation score was 3.

In the timing group, as hand-grip weakened, patients typically compensated by using their intrinsic hand muscles, as the more proximal muscles weakened first. Only one patient verbalized discomfort, and was unable to cough; anesthesia was promptly induced. The subsequent intubation score was 5. This patient had no postoperative recall of any discomfort. All other patients demonstrated adequate cough just prior to induction of anesthesia. Postoperatively no patients had recall of weakness and were very satisfied with their anesthetic technique.

**Discussion**

In this study we compared three techniques for rapid-sequence orotracheal intubation. The timing principle was investigated as an alternative to the priming principle. Intubating conditions present with priming were inferior to those present after succinylcholine, whereas intubating conditions present with timing were not. The degree of bucking was greater in the priming group than in the timing group. The similarity in twitch recovery times between timing and priming was expected since the total milligram-per-kilogram dose of vecuronium and of the maintenance anesthetic were similar in both groups.

The priming principle has been investigated extensively as an alternative for rapid tracheal intubation. This tech-
nique, depending on the priming or intubating doses and priming interval chosen, has been inconsistent in providing good intubating conditions. In addition to the increased incidence of bucking, the priming dose is also associated with diplopia, difficulty in swallowing, and inability to maintain head lift. Pulmonary aspiration also has been reported. Overall, the technique has a much higher incidence of coughing and bucking during intubation than that following succinylcholine.

Increasing the dose of nondepolarizing relaxant up to eight times the ED₉₅ has been shown to reduce the incidence of bucking and to significantly speed the onset of neuromuscular blockade. However, the recovery time from neuromuscular blockade using these methods is significantly prolonged.

The timing principle attempts to have the onset of peak neuromuscular blockade coincide with the onset of anesthesia. Since the onset of neuromuscular blockade takes longer than does the clinical onset of anesthesia, it is logical to administer the drugs in a sequence that coincides with their onset. Administration of any anesthetic drug to a patient with a full stomach places that patient at risk for aspiration. Therefore, when using the timing principle, all equipment used for airway management should be ready before administration of the muscle relaxant. Patients should be breathing oxygen, and Sellick’s maneuver should be used. Most importantly, it is necessary to explain to the patient that weakness will be experienced. This caveat should apply to the priming principle as well. In fact, a defasciculating dose of a nondepolarizing muscle relaxant before the administration of succinylcholine may also cause unpleasant side effects.

The priming principle uses a predetermined small dose of muscle relaxant administered prior to a larger intubating dose. Studies have confirmed that the side effects of muscle weakness are variable. The timing principle, on the other hand, individualizes the induction sequence with respect to the onset of muscle weakness in each patient. In addition, patients are aware that they will experience weakness in hand grip. Only one timing patient in our study experienced discomfort during induction. The remainder were able to breathe adequately until anesthesia was induced and did not experience unpleasant side effects. We attribute this to adequate preinduction preparation for the timing principle as well as to appropriate sedation. It is not surprising that most of the timing patients maintained adequate respiratory function, since the muscles of respiration and those of the upper airway are relatively resistant to neuromuscular blockade.

We did not attempt to quantify train-of-four measurements with an electromyogram or a force transducer. Instead, the goal of the study was to evaluate clinical intubating conditions in each of the three techniques. In fact, visual train-of-four measurements could not be correlated with intubation score in either timing or priming groups.

The results of our study should not be extrapolated to patients who receive different priming doses at different intervals than those used in this study. Furthermore, these results do not necessarily apply to muscle relaxants other than vecuronium. All of our patients received equal doses of vecuronium on a milligram-per-kilogram basis. The 4-min priming interval may be optimal with respect to intubating conditions and to shortening the time to maximal twitch depression.

In conclusion, we have shown that when compared to succinylcholine, intubating conditions using the timing principle are similar. The timing principle, from a pharmacodynamic viewpoint, is logical; a given endpoint of clinical weakness is achieved before anesthesia is induced. We feel that as long as the patient understands that weakness will occur, it does not present a problem. It is the patient who is unaware of impending paralysis who may become agitated. However, timing may not be appropriate for patients who can not cooperate or understand (i.e., intoxicated, obtunded, extremely agitated). The timing principle provides another method for administration of nondepolarizing muscle relaxants for rapid tracheal intubation. Timing, although similar, did not match the almost uniformly excellent intubating conditions of succinylcholine, and its use, therefore, is limited to cases where succinylcholine may be contraindicated or controversial.

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References


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