surgery be postponed. We monitor end-tidal carbon dioxide in all anesthetized patients by mass spectrometry, and hemoglobin saturation with pulse oximetry. We do not always measure blood gas tensions if there is no change in end-tidal CO_2 concentration and arterial O_2 saturation. Ideally, CPK should be measured at intervals (since the level may peak in 12–24 h), and urine should be examined for myoglobin after an episode of masseter spasm. However, these measurements have not always been made in our department because of uncertainty over their significance.

In summary, we found that masseter spasm is common in children anesthetized with halothane followed by succinylcholine. Our incidence of 1.02% agrees with that reported previously by Schwartz *et al.*[3] When halothane-succinylcholine is used in children with strabismus, masseter spasm is even more common: the incidence in our study (2.8%) was fourfold greater than that in children without strabismus. Several authors[2,5,6] have reported that the results from contracture testing demonstrate MH susceptibility in more than half of the children who have had an episode of masseter spasm. Thus, until the relation between these two conditions is clarified, we recommend muscle biopsy and contracture testing for children who experience masseter spasm.

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Heart Rate and Rhythm Following an Edrophonium/atropine Mixture for Antagonism of Neuromuscular Blockade during Fentanyl/N_2O/O_2 or Isoflurane/N_2O/O_2 Anesthesia

MURRAY L. URQUHART, M.D.,* FREDERIC M. RAMSEY, M.D.,† ROGER L. ROYSTER, M.D.,‡
ROBERT C. MORELL, M.D.,§ PAT GERR, C.R.N.A.¶

The efficacy and sustained duration of antagonism of neuromuscular blockade by edrophonium has become widely accepted since the initial reports of its use by Kopman[1] and Bevan.[2] Its rapid onset of action and reduced atropine requirement may make edrophonium preferable to the use of neostigmine or pyridostigmine,[3–6] and the drug of choice for antagonism of atracurium and vecuronium.[6–8]

Azar *et al.* demonstrated that administration of an edrophonium-atropine mixture produced superior heart rate stability when compared to administration of an edrophonium-glycopyrrolate mixture.[9] Cronnelly *et al.* demonstrated that the simultaneous administration of 0.5 mg/kg of edrophonium and 7 μg/kg of atropine produced fewer changes in heart rate than either neostigmine and atropine or edrophonium, and higher doses (15 μg/kg or 30 μg/kg) of atropine.[4] Both studies reported the occurrence of dysrhythmias after the administration of an edrophonium-atropine mixture. Miller and Cronnelly[3] suggested, in their 1983 editorial, that further study of the action of edrophonium was required, including a critical look at the assumption

* Instructor in Anesthesia.
† Associate Professor of Anesthesia.
‡ Assistant Professor of Anesthesia.
§ Resident in Anesthesia.
¶ Certified Registered Nurse Anesthetist.

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Address reprint requests to Dr. Ramsey: Department of Anesthesia, Massachusetts Eye and Ear Infirmary, 243 Charles Street, Boston, Massachusetts 02114.

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that its lower atropine requirement was associated with fewer dysrhythmias. This study was designed to compare the efficacy and safety of a constant dose ratio mixture of edrophonium and atropine in patients receiving either fentanyl-N_2O-O_2 or isoflurane-N_2O-O_2 anesthesia.

METHODS

The study was approved by the institution's Clinical Research Practices committee. Fifty-five patients, all ASA physical status I or II, were studied after giving informed consent. Patients with known cardiovascular disease, electrocardiographic evidence of dysrhythmias or atrioventricular (A–V) block, or receiving beta-adrenergic blocking drugs were excluded.

After oral premedication with diazepam, patients were randomly assigned to receive either fentanyl (group I, n = 26) or isoflurane (group II, n = 29) based anesthesia. Patients in group I received 5 μg/kg of fentanyl immediately prior to induction of anesthesia. Anesthesia was induced in all patients with thiopental (3–5 mg/kg). Neuromuscular function was measured by delivering supramaximal square wave pulses of 0.20 ms duration in a train-of-four (T4) configuration at 0.1 Hz to the ulnar nerve and measuring the force of thumb adduction with a Grass FT10 force displacement transducer, the results recorded on a Grass polygraph. Patients received an intubating dose of a nondepolarizing neuromuscular blocking drug (vecuronium 0.1 mg/kg; n = 24; atracurium 0.4 mg/kg, n = 30; pancuronium 0.1/mg/kg, n = 1), and the trachea was intubated after twitch depression reached 95% or greater. Anesthesia was maintained with 60% N_2O in oxygen, supplemental doses of relaxant, and either 0.5–1.5% isoflurane or additional doses of fentanyl (50–200 μg), depending on the group to which the patient was assigned. Lead II of the ECG was monitored throughout the procedure, and rhythm strips were obtained from a strip chart recorder. End-tidal anesthetic and CO_2 concentrations were measured continuously by mass spectrometry, and the patient's axillary temperature was monitored and maintained. Five to ten minutes prior to the end of surgery, arterial blood gases were measured.

At the end of surgery, isoflurane was discontinued, and twitch height as a percent of control, as well as heart rate, were measured. Two minutes thereafter, patients received 0.05–0.12 ml/kg of a solution containing 10 mg/ml of edrophonium and 0.140 mg/ml of atropine (OH101).** The initial dose was left to the clinical judgement of the staff anesthesiologist, and usually corresponded to the dose of 0.5 mg/kg of edrophonium and 7 μg/kg of atropine. A continuous recording of lead II of the ECG was obtained, and heart rate was recorded at 1-minute intervals for 10 min after the drug combination was given. Time to 95% of control twitch height and the height of the fourth twitch compared to the first (T4 ratio) were also recorded. Patients received additional OH101 if recovery of neuromuscular function reached a plateau before the twitch height had reached 95% of control after 10 min. The maximum allowable dose of OH101 was 0.12 ml/kg (1.2 ml/kg of edrophonium with 16.8 μg/kg of atropine). Patients received additional atropine (0.4 mg) at the discretion of the staff anesthesiologist if hemodynamically significant bradycardia or dysrhythmias occurred. After adequate recovery of neuromuscular function and emergence from anesthesia, the patients trachea was extubated. Adequacy of sustained recovery was monitored in the postanesthesia care unit for at least 2 h postoperatively by checking hand grip and sustained head lift for 5 s at frequent intervals.

In conjunction with a cardiologist, dysrhythmias were diagnosed by inspection of the rhythm strips obtained before and after antagonism of the neuromuscular block. First degree A–V block was diagnosed by a P–R interval increasing to greater than 0.20 msec after administration of OH101. Sinus bradycardia related to edrophonium was defined as a heart rate less than 50 bpm and at least 15% slower than heart rate immediately prior to administration of OH101. Severity of dysrhythmias for comparative purposes were classified as serious (2nd and 3rd degree A-V block, ventricular ectopy), moderate (bradycardia with a heart rate of more than 40 bpm, 1st degree A-V block), or mild (junctional rhythm, premature atrial contractions, new P wave focus).

The significance of factors affecting the heart rate following antagonism of neuromuscular blockade was tested for by analysis of variance for repeated measures. Repeated *t* tests were then used to find differences in heart rate between the two groups at each time period after antagonism. The Kaplan-Meir product limit estimation method was used to test for significance between the time to 95% recovery and the depth of block when OH101 was administered.[10] Chi-square analysis was used to determine the impact of the type of anesthesia on the incidence and severity of dysrhythmias. In addition, Chi-square analysis was employed to test for differences between groups for categorical variables (*i.e.*, sex, type of relaxant administered) and the *t* test for continuous variables (*i.e.*, age, weight). *P* values of less than 0.05 were considered significant.

** Anaquest, Division of BOC, Inc. Madison, Wisconsin.

RESULTS

Patients receiving either fentanyl (group I) or isoflurane (group II) anesthesia did not differ in terms of age, weight, sex, resting heart rate, or type of relaxant received (table 1). In addition, there was no significant difference in mean arterial blood gas values or mean axillary temperature between the two groups at the time of OH101 administration. Neuromuscular blockade was adequately antagonized in all patients by a dose of the mixture less than the maximum allowed by the protocol. All patients had their tracheas extubated in the operating room and had sustained neuromuscular function in the recovery room, as evidenced by hand grip and head lift.

The average time to 95% recovery of neuromuscular function for all patients was 6.98 min (SD of 4.1 min). The time to 95% recovery of twitch height was longer if antagonism was attempted before patients had spontaneously recovered 20% of control neuromuscular function (9.64 ± 6.69 min) than if attempted after 20% spontaneous recovery (4.93 ± 2.56 min) ($P = .001$).

The changes in heart rate after antagonism are shown for the two types of anesthesia in figure 1. There was no significant difference in baseline heart rates prior to antagonism between the two groups. Within group II, there was no statistically significant change in heart rate after administration of the antagonist mixture. In group I, there was a significant decline in mean heart rate at 1 and 2 min after antagonism of neuromuscular blockade compared to the heart rate immediately prior to administration of the mixture ($P < 0.01$).

The type and incidence of dysrhythmias or conduction blockade are shown in table 2. The type of anesthesia was related to the incidence of dysrhythmias ($P = 0.01$), while age, sex, resting heart rate, and heart rate immediately prior to reversal of neuromuscular blockade were not. There were no differences in arterial blood gas values or temperature between patients having an ECG abnormality and those who did not. Of patients receiving fentanyl anesthesia, 69.2% had a rhythm abnormality (predominantly sinus bradycardia and A–V block), while 34.5% of patients receiving isoflurane anesthesia had an abnormality (predominately junctional rhythm). More serious dysrhythmias had a significantly higher incidence in the fentanyl group. There was no significant difference in the incidence of dysrhythmias among patients receiving two doses of OH101 compared to those receiving only one dose. Only five patients received specific treatment for an ECG abnormality: four patients received additional atropine intravenously for either bradycardia or A-V block, and one patient received lidocaine intravenously for ventricular bigeminy. All but one of these patients were in group I, and all five patients responded promptly to treatment. No patient had any cardiovascular sequelae postoperatively.

TABLE 1. Demographic Data (Mean ± SD)

	Group I	Group II
N	26	29
Age (yr)	37.0 (14.0)	40.2 (13.5)
Weight (kg)	66.1 (13.7)	69.4 (15.5)
Resting heart rate (bpm)	75.8 (10.8)	75.0 (6.3)
% Female patients	62	62
Relaxant:		
Atracurium	17	13
Vecuronium	9	15
Arterial Blood Gas Values		
*p*H	7.42 (0.05)	7.42 (0.06)
P_{O_2} (mmHg)	119.4 (28.89)	159.3 (54.27)
P_{CO_2} (mmHg)	33.99 (3.71)	34.42 (5.44)
Serum potassium (meq/L)	4.27 (0.31)	4.15 (0.44)
Body temperature at antagonism (°C)	34.99 (0.65)	34.96 (0.76)

DISCUSSION

Our study confirms the clinical efficacy of antagonism of neuromuscular blockade with edrophonium. All 55 patients in the study had sufficient recovery of neuromuscular function to allow tracheal extubation, and all sustained adequate function postoperatively. Edrophonium was equally effective whether patients received fentanyl or isoflurane, and was equally effective in antagonizing the block of vecuronium or atracu-

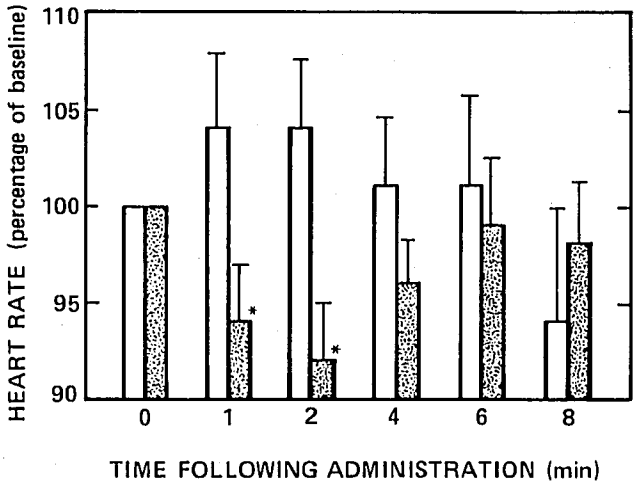

FIG. 1. Heart rate response (mean ± SEM) following antagonism of neuromuscular blockade with an edrophonium and atropine mixture (OH101). Open bars represent patients in group II (isoflurane anesthesia); stippled bars represent patients in group I (fentanyl anesthesia). *Values significantly different than baseline and significant differences between groups ($P < 0.05$).

TABLE 2. Incidence of Dysrhythmias

Dysrhythmias	Group I	Group II
None	8*	19
Severe	8*	3
2nd and 3rd degree AV block	6*	1
Ventricular dysrhythmia	1	1
Heart rate < 40 bpm	1	1
Moderate	7	4
Sinus bradycardia	4	3
1st degree AV block	3	1
Mild	3	3
Junctional rhythm	2	3
P wave change	1	0

* $P < 0.01$ between groups I and II.

rium. Our results agree with those of other authors that antagonism of blockade with a fixed dose of edrophonium is less predictable if attempted at more profound levels of block.[1,5,11-13]

We found that the constant dose ratio mixture of edrophonium and atropine used in this study failed to produce significant changes in heart rate when given to patients receiving isoflurane anesthesia. These results agree with those of Cronnelly *et al.*,[4] who found that 0.5 mg/kg edrophonium combined with 7 μg/kg of atropine (an identical ratio) produced the most heart rate stability when given during halothane anesthesia. In contrast, we found significant decreases in heart rate 1 and 2 min after administration of the mixture in patients receiving fentanyl anesthesia. Azar *et al.*[9] reported no significant difference in heart rate after edrophonium and atropine between patients receiving enflurane and fentanyl-based anesthesia. It should be noted, however, that patients in their study received a much higher dose of atropine; indeed, all patients had a significantly higher rate 1 and 2 min after antagonism of neuromuscular blockade compared to baseline values. Interestingly, they reported two patients developing bradycardia of 35 beats/min in the edrophonium/glycopyrrolate subgroup: both patients had received fentanyl-based anesthesia. Of patients in our study, 52% had a dysrhythmia or A–V block after antagonism of neuromuscular blockade with the mixture. This is similar to the incidence of dysrhythmias reported in other published studies. Cronnelly *et al.*[4] reported a 57% incidence of nodal dysrhythmias and 40% incidence of atrial and nodal dysrhythmias in patients receiving 0.5 mg/kg of edrophonium with 15 and 7 mcg/kg of atropine, respectively, during halothane anesthesia. Azar, *et al.*[9] found that 53% of patients receiving edrophonium and glycopyrrolate and 36% of patients receiving edrophonium and atropine had dysrhythmias consisting of junctional rhythm, ectopic beats, wandering pacemaker, or A-V dissociation. Although they studied two subgroups of patients, one receiving enflurane and the other fentanyl anesthesia, they did not differentiate the incidence of dysrhythmias between the two groups.

In our study, the dysrhythmias seen during fentanyl anesthesia tended to be more severe than those seen during isoflurane anesthesia. Although many of the ECG abnormalities seen could potentially have comprised hemodynamic stability, most resolved spontaneously. Treatment of dysrhythmias was deemed necessary in only five patients, all of whom responded promptly and without sequelae.

Edrophonium slows conduction through the A-V node by potentiating parasympathetic tone; specifically, prolonging the time for the action potential to travel from the atria to the bundle of His.[14] It is known that the effect of a vagotonic intervention is influenced greatly by preexisting autonomic tone. Edrophonium's effect on the A-V node might, therefore, be expected to be greater when conduction is prolonged by preexisting influences. Indeed, the administration of neostigmine is associated with more profound bradycardia when given during halothane anesthesia than during enflurane anesthesia.[15] Halothane is known to have negative chronotropic effects and to prolong A-V nodal conduction.[16] The higher incidence of dysrhythmias and conduction blockade, and the statistically slower heart rates in patients receiving fentanyl in our study, suggest a similar additive effect of fentanyl and edrophonium at the A-V node. Recent studies in dogs at our institution show that fentanyl significantly slows A-V nodal conduction.[17] The results of this study offer experimental support to our clinical conclusion that fentanyl predisposes patients to vagally mediated ECG abnormalities by prolonging A-V nodal conduction. Isoflurane anesthesia has no effect on A-V nodal conduction, and would, therefore, not be expected to have an additive effect with edrophonium.[15]

In conclusion, we found edrophonium to be efficacious in antagonizing nondepolarizing neuromuscular blockade. When given simultaneously with a constant dose ratio of atropine, it was associated with a significant incidence of dysrhythmias, especially in patients receiving fentanyl anesthesia. In addition, patients receiving fentanyl anesthesia had significant slowing of heart rate following reversal. The dysrhythmias and bradycardia we noted were infrequently of hemodynamic consequence. We suggest, however, that use of a constant dose ratio combination of edrophonium and atropine should be used with caution in patients at increased risk of morbidity from sinus bradycardia, A-V nodal conduction blockade, or other dysrhythmias. The optimal amount of atropine required to prevent musca-

rinic side effects following antagonism of neuromuscular blockade with edrophonium may depend on the anesthetic administered, the dose of edrophonium given, and the medical condition of the patient.

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Unexpected Migration of an Esophageal Foreign Body

MICHAEL GRESCHNER, M.Sc., M.D.C.M.,* J. HUGH DEVITT, M.D., M.Sc., F.R.C.P.(C.)†

One of the contraindications to the use of Sellick's maneuver is the presence of a foreign body in the esophagus.[1] The precise localization of an esophageal foreign body is critical in planning the anaesthetic.

* Resident in Anaesthesia.
† Staff Anaesthetist.

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Address reprint requests to Dr Devitt: Department of Anaesthesia, Sunnybrook Medical Centre, 2075 Bayview Avenue, Toronto, Ontario, M4N 3M5, Canada.

Key words: Airway: foreign body. Intubation: awake tracheal.

Report of a Case

A 33 yr-old woman with a long psychiatric history of a chronic personality disorder with depressive reaction was admitted to hospital 5 h after swallowing two open safety pins, complaining of chest pain and abdominal discomfort. The patient had a previous history of multiple hospitalizations for removal of foreign bodies from her gastrointestinal tract. On admission, the pain was retrosternal in nature without any radiation. The patient denied symptoms of nausea, vomiting, retching, dyspnea, cough, fever, or chills. The rest of the history was unremarkable. Her last oral intake was 7 h prior to admission.

Physical examination revealed an arterial blood pressure of 116/70 mmHg with a heart rate of 92 bpm and respiratory rate of 18 breaths/min. The remainder of the physical examination at admission was normal. Laboratory investigation was unremarkable. Soft tissue roentgenograms of the neck demonstrated an open safety pin adjacent