

The Heart Rate Following Edrophonium-Atropine and Edrophonium-Glycopyrrolate Mixtures

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Contrary to a long-standing belief, edrophonium recently has been shown to be an effective antagonist of nondepolarizing muscle relaxants with an onset of action faster than either that of neostigmine or pyridostigmine¹⁻³ and with a similar duration of action as that of neostigmine.^{4,5}

Neostigmine-glycopyrrolate (NG) mixture has been shown to cause less tachycardia than neostigmine-atropine (NA) mixture during reversal of muscle relaxants.⁶⁻¹⁰ The heart-rate response to edrophonium-anticholinergic combinations has not been reported as yet. This study compares the effect of edrophonium-atropine (EA) and edrophonium-glycopyrrolate (EG) mixtures on the heart rate during reversal of pancuronium in anesthetized patients.

METHOD

The study was approved by the institutional Committee on Scientific Activities. Informed consent was obtained from 90 patients scheduled for abdominal surgery under general anesthesia. All patients were ASA class I or II and without significant cardiovascular disorders. The patients were premedicated with meperidine 0.5-1 mg/kg, droperidol 2.5 mg or hydroxyzine 50 mg, and atropine 0.5 mg, given intramuscularly 60-90 min before the induction of anesthesia. Anesthesia was induced with sodium thiopental, 4 mg/kg iv, and the trachea was intubated following succinylcholine 1-1.5 mg/kg iv. Pancuronium, 0.04-0.08 mg/kg iv, was given to facilitate muscular relaxation during surgery.

Sixty patients were anesthetized with enflurane, inspiratory concentration 1-1.5%, in nitrous oxide 50-60%, and 30 patients received balanced anesthesia con-

sisting of nitrous oxide 60-70% and intermittent doses of fentanyl, total 0.25-0.75 mg. At the conclusion of surgery, all patients received edrophonium 0.5 mg/kg combined with either glycopyrrolate 0.5 mg (n = 45) or atropine 1 mg (n = 45) intravenously. The standard lead II of the ECG was recorded continuously during the reversal and the heart rate was determined electronically every minute on the minute for a minimum of 5 min after the administration of either mixture. Nitrous oxide administration was continued and patient stimulation was avoided during reversal and until the study was completed.

The results were analyzed by Student's paired *t* test. *P* values less than 0.05 were considered significant.

RESULTS

Sixty-eight female patients and 22 male patients, mean age 45 years and mean weight 65 kg, were studied. The changes in the heart rate are summarized in figure 1. By 1 min after the administration of the EA mixture, the heart rate had increased by 0-34 beats/min and then decreased by 1-20 beats/min and remained stable for the remainder of the 5-min observation period. By 1 min after the administration of the EG mixture, the heart rate had decreased by 0-23 beats/min and then increased by 1-34 beats/min and remained stable for the remainder of the 5-min observation period. The heart rates in the balanced anesthesia subgroups usually were lower than in the enflurane subgroups, but the changes in the heart rates were of similar magnitude and direction. Two patients in the balanced anesthesia subgroup developed bradycardia of 35 beats/min about a minute after the administration of EG mixture and required treatment with atropine.

Dysrhythmias were observed in all four subgroups during the reversal. Junctional rhythm, wandering pacemaker, and premature atrial contractions occurred in 12, four, and eight patients in the EG group and in 10, four and two patients in the EA group, respectively. Occasional premature ventricular contractions occurred in four patients in the EA group and prolonged PR interval in one patient in each group. The dysrhythmias lasted 1-3 min.

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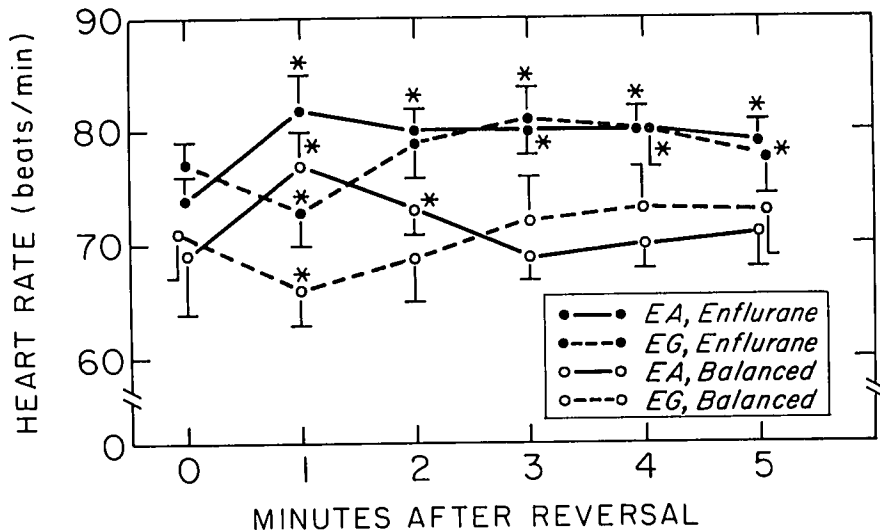


FIG. 1. The heart rate (HR) in beats/min (mean standard error) following edrophonium-atropine (EA) and edrophonium-glycopyrrolate (EG) mixtures. * $P < 0.05$ when compared with the heart rate just before the administration of the reversal mixture.

DISCUSSION

A significant increase in the heart rate occurs during reversal of muscle relaxants with NA combinations. Atropine may increase the heart rate by up to 45% when compared with prereversal values.^{6-9,11-13} When atropine is replaced with glycopyrrolate, only small changes occur in the heart rate.⁶⁻¹⁰ Therefore, NG combinations are considered superior to NA combinations for reversal of muscle relaxants.

In contrast to neostigmine-anticholinergic combinations, our study suggests that EA mixture is superior to EG mixture: EA caused a moderate increase in the heart rate, while EG often decreased the heart rate and occasionally caused severe bradycardia.

The effect of a reversal mixture on the heart rate probably is related to the onset of action of each individual drug in the mixture. Edrophonium and atropine have a rapid onset,^{2,4,7,10} while neostigmine and glycopyrrolate have a slow onset.^{4,7,9,10,13} The onset of the cholinergic effects of edrophonium and neostigmine coincides with the onset of the anticholinergic effects of atropine and glycopyrrolate, respectively. Thus, when properly matched, these agents produce minimal changes in the heart rate.

EA mixture also is superior to EG mixture because edrophonium and atropine have similar duration of action.¹⁴⁻¹⁶ When the long-acting neostigmine is combined with the short-acting atropine, often late bradycardia occurs.⁹ This is reduced greatly when atropine is replaced by the long-acting glycopyrrolate.⁹ It is conceivable that the incidence of late changes in the heart rate following administration of EA mixture would be low because edrophonium and atropine have a similar duration of action.

Dysrhythmias, primarily junctional rhythm, ectopic beats, wandering pacemaker, and A-V dissociation, have been reported following NA and NG combinations.^{6,7,10,17} We have observed similar dysrhythmias in both the EA and EG groups.

In summary, the administration of the EA mixture had a minimal effect on the heart rate, while the EG mixture often caused a decrease in the heart rate and occasionally severe bradycardia. The EA mixture is superior to the EG mixture because atropine and edrophonium have a similar onset and duration of action, while glycopyrrolate has a longer onset and duration of action than edrophonium.

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Venospasm Preventing Peripheral Venous Access

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Venospasm is a poorly understood phenomenon that occurs primarily at the time of central vein or right heart catheterization. We report a case in which venospasm occurred with insertion of a peripheral intravenous catheter, preventing venous access in an anesthetized patient.

REPORT OF A CASE

An eleven-year-old boy with cerebral palsy, mental retardation, and congenital hydrocephalus with a functioning ventriculoperitoneal shunt was scheduled to have hip and knee releases for spasticity of the lower extremities. The patient previously had numerous general anesthetics at different hospitals, from which no old records were available. The only previous anesthetic problem related by the parents was that the patient required prolonged postoperative endotracheal intubation on one occasion for what apparently was postintubation croup. The patient was receiving no medications and had no known allergies. Physical examination revealed no cardiovascular abnormalities. Laboratory examination was unremarkable.

The patient was premedicated with atropine 0.4 mg po. An inhalation induction of anesthesia was performed with nitrous oxide and gradually increasing halothane concentrations. Following induction, a 20-gauge, 32-mm Teflon® intravenous catheter (Critikon Cathlon IV) was inserted easily into a vein on the dorsum of the left hand.

There was good blood return initially through the catheter before and after removal of the obturator, but the intravenous solution, consisting of 5% dextrose in lactated Ringer's solution (D₅LR), would not flow. Flushing of the catheter with a 3-ml syringe was attempted but was not possible using moderate force, even when the catheter was withdrawn almost out of the vein and readvanced several times. Attempted flushing produced only a blanching of the skin around the tip of the catheter accompanied by a localized wheal 2 cm in diameter that resembled an intradermal injection, having the characteristic "orange skin" appearance. Backflow of blood no longer occurred when the syringe was disconnected from the catheter.

A similar 20-gauge intravenous catheter then was inserted into a vein in the dorsum of the right hand, again without difficulty. There was free flow of blood through the catheter, but upon attempted infusion of the intravenous solution with a different bottle of D₅LR there was no flow. Flushing and withdrawing of the catheter was attempted, producing the same results as on the previous occasion. Two per cent lidocaine was injected into each of the catheters in the hands. Injection of 0.2 ml into each catheter was difficult, requiring significant force applied to a 3-ml syringe for 10-15 seconds and causing no change in venospasm. The left external jugular vein then was cannulated with a 20-gauge catheter, through which the same intravenous crystalloid flowed readily. Endotracheal intubation then was performed with the aid of succinylcholine, and the remainder of the operative course was uneventful.

The peripheral catheters were removed at the conclusion of the case after it was apparent that the venospasm would not relax before emergence from anesthesia. Inspection of the catheters showed that they were not crimped. The postoperative course was uneventful. Postoperative inspection of venipuncture sites revealed no evidence of inflammation or other abnormalities.

DISCUSSION

Venospasm occurs with central vein and right heart catheterization via peripheral veins. One study in which 4,413 right heart catheterizations were performed re-

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