

The Effect of a Second Dose of Succinylcholine on Cardiac Rate and Rhythm Following Induction of Anesthesia with Etomidate or Midazolam

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Since its introduction into anesthetic practice, succinylcholine (SCh) has been the subject of widespread study and discussion regarding its effects on cardiac rate and rhythm. Marked dysrhythmias (usually transient asystole and nodal rhythm) following a second injection of succinylcholine consistently occur in adults after inhaled anesthetic induction with halothane and nitrous oxide.^{1,2} The use of thiopental for anesthetic induction protects against the occurrence of such dysrhythmias.^{1,2}

Whether the two newer intravenous induction agents, etomidate and midazolam, also exhibit a protective effect against SCh-induced dysrhythmias has not been previously investigated. This study was undertaken to define the effect of a second SCh injection after anesthetic induction with etomidate or midazolam.

MATERIALS AND METHODS

Four groups of ASA class I patients with a mean age of 33 yr (range 19–67 yr) undergoing elective surgical procedures were studied. Approval of the Human Subjects Protection Committee at our institution was obtained. Details of the study protocol and the risks involved in participating in this study were fully explained to the patients, and informed consent was obtained. The study protocol and the anesthetic procedure are shown in figure 1. All patients received morphine sulfate 0.15 mg/kg im 1 h before induction. After breathing oxygen for 3 min, anesthesia was induced with etomidate (0.3 mg/kg) iv in groups I (n = 8) and IV (n = 6), midazolam (0.4 mg/kg) in group II (n = 9), and thiopental (5 mg/kg) in group III (n = 8). After abolition of the eyelash reflex, SCh 1 mg/kg iv was given to all groups. Following endotracheal intubation, con-

trolled ventilation with N₂O in O₂ (4:2) was instituted, and no further stimulation was allowed for the duration of the observations. Five minutes after the first SCh injection, a second dose (0.5 mg/kg) was administered. In group IV, atropine (0.01 mg/kg) iv was given 30 s before the second dose of SCh. ECG lead II was continuously monitored and recorded during the observation period. Arterial blood pressure was measured every minute using an automated blood pressure machine, and blood oxygen saturation was continuously monitored using a pulse oximeter. Heart rate (HR) was calculated from the R-R interval. Unpaired student's *t* test and Fisher exact test were used for statistical analysis, with *P* < 0.05 considered to be significant.

RESULTS

The results are given in table 1. The decrease in HR after the second injection of SCh was not significant in the etomidate-atropine group, while a significant decrease was observed in the etomidate, midazolam, and thiopental groups as compared with HR immediately prior to the second injection. Sinus arrest with nodal escape rhythm occurred in six patients in the etomidate group (the time from the last P-wave to the recurrence of a P-wave after the escape beats was 3.5 s ± 0.2), and in one patient in the midazolam group (3.2 s). Nodal rhythm at a rate of 47 bpm for 45 s developed in one patient in the etomidate group, and occurred at a rate of 43 bpm for 40 s in one patient in the midazolam group. None of the patients in the etomidate-atropine and thiopental groups exhibited any dysrhythmias. As compared to the thiopental group, the occurrence of dysrhythmias (transient sinus arrest with nodal escape rhythm and nodal rhythm) was statistically significant in the etomidate group while it was not in the midazolam group. All dysrhythmias occurred 25–30 s after the second dose of SCh, and resolved spontaneously within 60 s. All patients in this study had an uncomplicated perioperative course. Figure 2 shows the ECG of a patient in the etomidate group.

DISCUSSION

Our results confirmed that thiopental protects against dysrhythmias induced by a second dose of SCh

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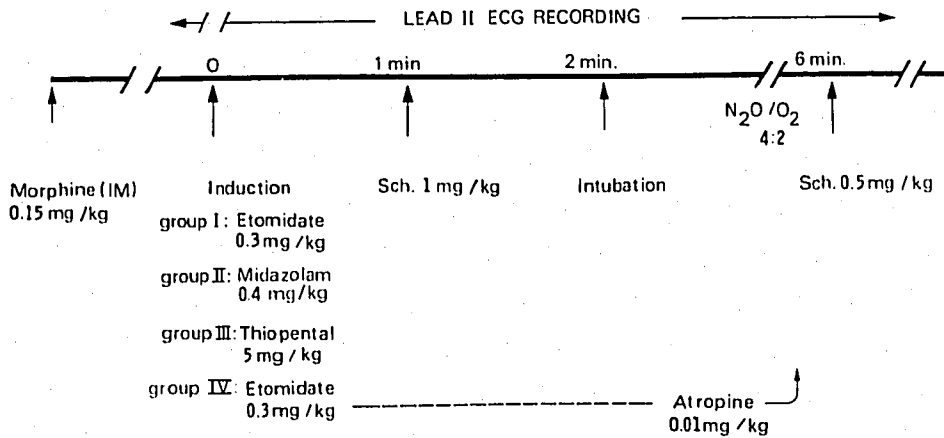


FIG. 1. The study protocol and the anesthetic procedure.

administered 5 min after the first dose, in agreement with the findings of Schoenstadt and Whitcher.² Our data are also consistent with that of Stoelting and Peterson,³ who showed that a significant decrease in HR occurred after a second dose of SCh in patients induced with thiamylal. This study showed that etomidate does not possess a protective effect against SCh-induced dysrhythmias, while midazolam exhibits a variable effect (although the occurrence of dysrhythmias in this group was not statistically significant).

The mechanism by which dysrhythmias are induced following a second injection of SCh has not been clearly defined. Enhanced vagal activity is suggested because a protective effect is observed when iv atropine⁴ or glycopyrrolate⁵ is given prior to a second dose of SCh. Schoenstadt and Whitcher² postulated that "sensitization" occurs to the second injection of SCh by the choline formed in the hydrolysis of the first injection of

SCh. More recently, Nigrovic, in a theoretical analysis,⁶ hypothesized that activation of presynaptic muscarinic receptors on the sympathetic nerve terminals inhibits the release of norepinephrine, while activation of presynaptic nicotinic receptors leads to release of norepinephrine. He postulated that activation of these cholinergic receptors, as well as postsynaptic muscarinic receptors at the sino-atrial node by a single injection of SCh, results in opposing effects with a net small and variable effect on the heart rate. Furthermore, he hypothesized that bradycardias may occur following a second injection of SCh, because the muscarinic receptors around the sinoatrial node and the presynaptic muscarinic receptors are again activated, while the nicotinic receptors remain desensitized from the first dose.

The mechanism by which thiopental protects against marked dysrhythmias following a second dose of SCh is also not well defined, but it has been postulated to be

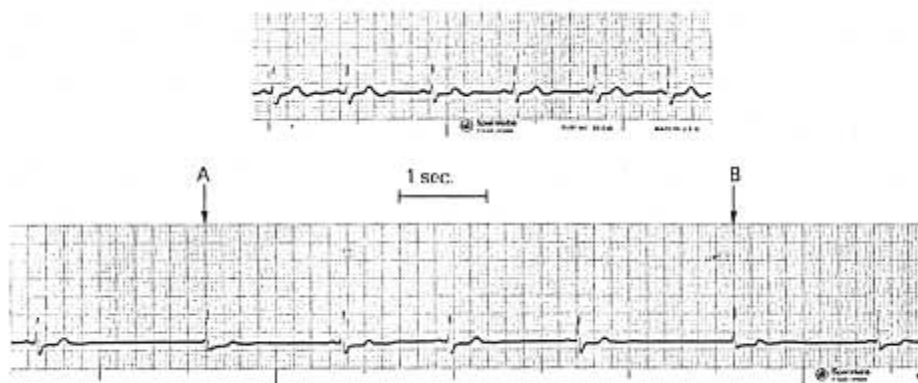
TABLE 1. Effect of Second Dose of Succinylcholine on Cardiac Rate and Rhythm

Group	Age (Yr)	Baseline HR	HR Before 2nd SCh	Minimum HR After 2nd SCh	Rhythm After 2nd SCh
I Etomidate n = 8	31 ± 10	77 ± 15	93 ± 20	34* ± 21	<ul style="list-style-type: none"> • Sinus arrest (3.5 ± 0.2 s) with nodal escape rhythm (n = 6). • Nodal rhythm at a rate of 47 bpm for 45 s (n = 1).
II Midazolam n = 9	34 ± 11	84 ± 23	103 ± 12	70* ± 31	<ul style="list-style-type: none"> • Sinus rhythm (n = 1). • Sinus arrest (3.2 s) with nodal escape rhythm (n = 1). • Nodal rhythm at a rate of 43 bpm for 40 s (n = 1).
III Thiopental n = 8	38 ± 13	76 ± 15	92 ± 16	75* ± 08	<ul style="list-style-type: none"> • Sinus rhythm (n = 7). • Sinus rhythm (n = 8).
IV Etomidate-Atropine n = 6	30 ± 05	69 ± 13	92 ± 16	78 ± 24	<ul style="list-style-type: none"> • Sinus rhythm (n = 6).

Values are mean ± SD; n = number of patients; HR = heart rate (bpm); SCh = succinylcholine.

* $P < 0.05$ as compared to HR before 2nd SCh.

FIG. 2. ECG tracings before and after second dose of SCh following induction with etomidate. Upper tracing—heart rate 63/min immediately before second dose of SCh. Lower tracing—25 s after second dose of SCh. Sinus arrest for 3.4 s and nodal escape after 1.9 s (A) and 1.8 s (B). Minimum HR = 31 bpm.



due to its vagolytic properties. Greenberg *et al.*⁷ showed that pentobarbital, atropine, or bilateral vagotomy antagonizes digoxin-induced bradycardia in dogs. Page and McCubbin⁸ found that pentobarbital, like atropine, largely eliminates parasympathetic compensatory reflexes in response to vasoactive substances. The fact that barbiturates (including thiopental) remain the most commonly used agents for anesthetic induction in adults likely accounts for the apparent low incidence in clinical practice of marked dysrhythmias following repeated doses of SCh.

Brandt and Viby-Mogensen⁴ concluded that, when an inhaled anesthetic induction with nitrous oxide and halothane is used, intravenous atropine in a dose not exceeding 0.01 mg/kg should precede a second dose of SCh to protect against SCh-induced dysrhythmias. These workers and others had previously shown that intramuscular atropine does not protect against dysrhythmias following a second succinylcholine dose.^{3,9} Our results demonstrated that, after induction with etomidate, intravenous administration of atropine is necessary to protect against dysrhythmias following a second injection of SCh. Therefore, it seems reasonable to assume that etomidate, in contrast to thiopental, lacks significant vagolytic activity. Midazolam may possess a lesser vagolytic effect, since the second dose of SCh produced inconsistent dysrhythmias. Further study is required to define the vagolytic properties of etomidate and midazolam.

The present experience suggests that, after anesthetic induction with etomidate, particularly in patients

who may suffer deleterious effects from dysrhythmias or bradycardia, administration of iv atropine should be considered prior to a second injection of SCh.

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