It is not necessary to administer more than $10 \mu\text{g} \cdot \text{kg}^{-1}$ of atropine to older children before succinylcholine

G.D. Shorten MD, B. Bissonnette MD, E. Hartley MD,
W. Nelson MD, A.S. Carr FRCA

It is common practice at the Hospital for Sick Children, Toronto, to administer atropine $20 \mu\text{g} \cdot \text{kg}^{-1}$ prior to succinylcholine in infants and children. It is unclear whether "prophylactic" administration of this dose of atropine to older children (6–16 yr) is necessary. This study was designed to compare the changes in heart rate, rhythm and mean arterial pressure after administration of either atropine 10 or $20 \mu\text{g} \cdot \text{kg}^{-1}$ with succinylcholine or vecuronium (control group) to older children anaesthetized with thiopentone. Thirty-six ASA I or II patients (6–16 yr) were studied. Anaesthesia was induced with thiopentone $5 \text{ mg} \cdot \text{kg}^{-1}$. Patients were randomly assigned to receive: (a) atropine $10 \mu\text{g} \cdot \text{kg}^{-1}$ and succinylcholine $1.5 \text{ mg} \cdot \text{kg}^{-1}$ ($n = 12$), (b) atropine $20 \mu\text{g} \cdot \text{kg}^{-1}$ and succinylcholine $1.5 \text{ mg} \cdot \text{kg}^{-1}$ ($n = 13$) or (c) vecuronium $0.1 \text{ mg} \cdot \text{kg}^{-1}$ ($n = 11$) to facilitate tracheal intubation. Heart rate and rhythm were recorded continuously using a computerised analogue interface whereas blood pressure was monitored non-invasively before induction of anaesthesia, immediately before and at one and three minutes after laryngoscopy. No difference was observed between patients who received atropine 10 or $20 \mu\text{g} \cdot \text{kg}^{-1}$ prior to succinylcholine. No episode of sinus bradycardia occurred. Premature atrial contractions were observed in two patients (one succinylcholine/atropine $20 \mu\text{g} \cdot \text{kg}^{-1}$, one vecuronium). Administration of atropine $20 \mu\text{g} \cdot \text{kg}^{-1}$ prior to succinylcholine

provides no advantage over atropine $10 \mu\text{g} \cdot \text{kg}^{-1}$ in older children in terms of cardiovascular stability.

A l'hôpital pour enfants malades de Toronto, il existe une pratique courante qui consiste à administrer de l'atropine $20 \mu\text{g} \cdot \text{kg}^{-1}$ avant la succinylcholine aux nourrissons et aux enfants. Il n'est pas évident que l'administration préventive d'atropine à cette dose soit nécessaire chez les enfants plus âgés (6–16 ans). Cette étude vise à comparer les changements de fréquence et de rythme cardiaques, et de pression artérielle moyenne après l'administration d'atropine 10 ou $20 \mu\text{g} \cdot \text{kg}^{-1}$ et de succinylcholine ou de vecuronium (groupe contrôle) chez des enfants plus âgés. Trente-six patients ASA I et II âgés de 6 à 16 ans font partie de l'étude. L'anesthésie est induite avec du thiopentone $5 \text{ mg} \cdot \text{kg}^{-1}$. Les patients sont répartis au hasard pour recevoir: a) de l'atropine $10 \mu\text{g} \cdot \text{kg}^{-1}$ et de la succinylcholine $1,5 \text{ mg} \cdot \text{kg}^{-1}$ ($n = 12$), b) atropine $20 \mu\text{g} \cdot \text{kg}^{-1}$ et succinylcholine $1,5 \text{ mg} \cdot \text{kg}^{-1}$ ($n = 13$), ou c) vecuronium $0,1 \text{ mg} \cdot \text{kg}^{-1}$ ($n = 11$) pour faciliter l'intubation de la trachée. La fréquence et le rythme cardiaque sont enregistrés en continu à l'aide d'une interface analogique alors que la pression artérielle est monitorée de façon non effractive avant l'induction de l'anesthésie, immédiatement avant la laryngoscopie et à une et trois minutes après la laryngoscopie. On n'observe pas de différences entre les patients qui reçoivent 10 μg ou $20 \mu\text{g} \cdot \text{kg}^{-1}$ avant la succinylcholine. Aucun épisode de bradycardie sinusale n'est relevé. Des contractions auriculaires prématurées ont été enregistrées chez deux patients (un avait reçu succinylcholine/atropine $20 \mu\text{g} \cdot \text{kg}^{-1}$, l'autre du vecuronium). L'administration d'atropine $20 \mu\text{g} \cdot \text{kg}^{-1}$ avant la succinylcholine ne présente pas d'avantages sur l'atropine $10 \mu\text{g} \cdot \text{kg}^{-1}$ administrée à des enfants plus âgés sous le rapport de la stabilité cardio-vasculaire.

Key words

ANAESTHESIA: paediatric;

ARRHYTHMIA: bradycardia, premature atrial contraction;

NEUROMUSCULAR RELAXANTS: succinylcholine, vecuronium;

PARASYMPATHETIC NERVOUS SYSTEM: atropine.

From the Department of Anaesthesia, The Hospital for Sick Children, University of Toronto, Toronto, Ontario, Canada, M5G 1X8.

Address correspondence to: Dr. B. Bissonnette, Department of Anaesthesia, The Hospital for Sick Children, Toronto, Ont. M5G 1X8, Canada.

Accepted for publication 19th August, 1994.

The risk of sinus bradycardia in infants and young children following a single dose of succinylcholine has been recognized for more than three decades.^{1,2} In adults, bradycardia does not occur unless a second dose of succinylcholine (particularly within five minutes of the first dose) is administered.^{3,4} It is common clinical practice

to administer atropine $20 \mu\text{g} \cdot \text{kg}^{-1}$ "prophylactically" prior to a first dose of succinylcholine in infants and young children, but not in adults. In this dose, atropine prevents succinylcholine-associated bradycardia in children aged one to seven years.⁵ It is unclear whether "prophylactic" administration of atropine in this dose is necessary in older children: atropine $10 \mu\text{g} \cdot \text{kg}^{-1}$ reduces but does not eliminate the incidence of succinylcholine-associated arrhythmias in infants.⁶ The objective of this study was to compare the changes in heart rate, rhythm and mean arterial pressure following administration of either atropine 10 or $20 \mu\text{g} \cdot \text{kg}^{-1}$ before succinylcholine to older children anaesthetised with thiopentone.

Methods

After obtaining approval from the Human Subject Review Committee and written informed parental consent, 36 ASA class I or II children aged 6–16 yr undergoing elective surgical procedures for which tracheal intubation was indicated, were studied. Patients were excluded if a history of neuromuscular disease, any condition predisposing to succinylcholine-induced hyperkalaemia or any medication known to influence neuromuscular function was obtained.

The children received no premedication. After arrival in the operating room, ECG and blood pressure monitors were applied and a record of two minutes of continuous ECG monitoring obtained. A 22G intravenous cannula was inserted. If necessary, 66% nitrous oxide in oxygen was administered by facemask to facilitate cannula placement. The study period extended from three minutes before induction of anaesthesia until five minutes after tracheal intubation. During this time heart rate and rhythm (lead II) were monitored and recorded continuously using an analogue interface system (AcqKnowledge v 2.1 – Biopac, Montreal, P.Q.). The blood pressure was monitored non-invasively (Hewlett Packard 78352A – Mississauga, Ontario) immediately before induction of anaesthesia and administration of muscle relaxant, immediately before laryngoscopy and at one and three minutes after laryngoscopy. Induction of anaesthesia consisted of the administration of thiopentone $5 \text{ mg} \cdot \text{kg}^{-1}$. Patients were randomly assigned to receive: (1) atropine $10 \mu\text{g} \cdot \text{kg}^{-1}$ and succinylcholine $1.5 \text{ mg} \cdot \text{kg}^{-1}$ (2) atropine $20 \mu\text{g} \cdot \text{kg}^{-1}$ and succinylcholine $1.5 \text{ mg} \cdot \text{kg}^{-1}$ or (3) vecuronium ($0.1 \text{ mg} \cdot \text{kg}^{-1}$) to allow tracheal intubation. Vecuronium was selected for comparison because of its cardiovascular stability in the paediatric population.^{7,8} Manual positive-pressure ventilation using a circle system (children $>20 \text{ kg}$) or Jackson-Rees modification of an Ayre's T-piece with 66% nitrous oxide in oxygen was instituted to maintain the oxygen saturation greater than 97% and the end-tidal partial pressure of CO_2 within normal limits

TABLE I Demographic data

Group	Age (yr)	Sex (M:F)	Weight (kg)
S/A 10 ($n = 12$)	11.6 (3.9)	6:6	45.2 (21.9)
S/A 20 ($n = 13$)	10.2 (2.5)	10:3*	42.5 (17.3)
Vec ($n = 11$)	9.2 (2.2)	6:5	29.7 (5.4)

Mean $\pm$ (SD); S/A 10: succinylcholine/atropine ($10 \mu\text{g} \cdot \text{kg}^{-1}$); S/A 20: succinylcholine/atropine ($20 \mu\text{g} \cdot \text{kg}^{-1}$); Vec: vecuronium.

* $P < 0.05$.

(35–45 mmHg). Sixty seconds after completion of the injection in both succinylcholine/atropine groups direct laryngoscopy and tracheal intubation were performed. Ninety seconds after completion of the injection in the vecuronium group a second dose of thiopentone $1 \text{ mg} \cdot \text{kg}^{-1}$ was administered through a fast-running intravenous infusion before the trachea was intubated.

Each electrocardiographic record was subsequently examined by one of the investigators who was unaware of the study group to which it belonged. The presence of arrhythmias was sought and the maximum changes in heart rate from pre-induction to pre-laryngoscopy and from pre-induction to post-laryngoscopy were calculated. For the purposes of this study, sinus bradycardia was defined as three or more sinus beats at a rate of $<60 \cdot \text{min}^{-1}$.

All data with parametric values are reported as mean $\pm$ standard deviation. The determination of the number of patients to be studied per group was achieved using a power analysis based on an $\alpha = 0.05$, $\beta = 0.2$ and an estimated incidence of succinylcholine-induced bradycardia in the 6–16-yr-old population of 30%. The calculated number of patients needed to reject the null hypothesis (i.e., reduce the incidence to zero) was 12 per group. Heart rate and mean arterial pressure data between groups were analysed using ANOVA and Student-Newman-Keuls for multiple comparisons whereas within-group data analysis was performed using repeated measure analysis. The incidence of arrhythmias was analysed using Fisher's exact test. $P < 0.05$ was accepted as statistically significant.

Results

Demographic data are reported in Table I. Although a greater proportion of patients who received atropine $20 \mu\text{g} \cdot \text{kg}^{-1}$ were male, this is unlikely to have influenced the results obtained (Table I).

Mean arterial pressure and heart rate data are summarized in Tables II and III. When compared with pre-induction values, heart rate and mean arterial pressure increased in both succinylcholine/atropine groups ($P < 0.05$) but not in the vecuronium group. The magnitude

TABLE II Mean arterial pressure (mmHg)

Group	Pre-induction	Post-induction	1 min post-laryngoscopy	3 min post-laryngoscopy
S/A 10	89.9 (16.8)	111 (14.5)	106.9 (13.9)	103.1 (16.6)
S/A 20	84.1 (11.5)	94.3 (15.2)	109.3 (19.3)	93.8 (17.8)
Vecuronium	96.6 (13.6)	92.8 (16.3)	115.4 (11.8)	98.4 (21.9)

Mean $\pm$ (SD); S/A 10: succinylcholine/atropine ($10 \mu\text{g} \cdot \text{kg}^{-1}$); S/A 20: succinylcholine/atropine ($20 \mu\text{g} \cdot \text{kg}^{-1}$).

of the increase in mean arterial pressure was greater in those who received atropine $10 \mu\text{g} \cdot \text{kg}^{-1}$ than in those who received atropine $20 \mu\text{g} \cdot \text{kg}^{-1}$ ($P < 0.05$). The magnitude of increase in heart rate was similar in the two succinylcholine atropine groups (Table IV). Compared with pre-induction values, heart rate and mean arterial pressure increased to a similar degree in all three groups after laryngoscopy and intubation (Table IV).

No episode of sinus bradycardia occurred. Premature atrial contractions were observed in two patients in the succinylcholine/atropine $20 \mu\text{g} \cdot \text{kg}^{-1}$ group and one in the vecuronium group. In two of the succinylcholine/atropine $20 \mu\text{g} \cdot \text{kg}^{-1}$ group and one of the vecuronium group, electrocardiographic tracings were considered inadequate for detection of non-sinus arrhythmias.

Discussion

Our data indicate that administration of atropine 10 or $20 \mu\text{g} \cdot \text{kg}^{-1}$ to older children (6–16 yr) before succinylcholine produces similar changes in heart rate and mean arterial pressure. Previously, the atropine dose-requirement for prevention of succinylcholine-induced bradycardia in this age group has not been studied.

Cardiac arrhythmias including sinus tachycardia,^{9,10} ventricular ectopic beats,¹⁰ ventricular bigeminy,¹⁰ sinus bradycardia⁹ and asystole¹¹ have been described following administration of succinylcholine to children. The establishment of a causal relationship between the administration of succinylcholine and these arrhythmias can be confounded by the presence of other potent arrhythmogenic factors such as an halogenated hydrocarbon volatile in the presence of circulating catecholamines,¹² laryngoscopy and tracheal intubation (particularly during "light" anaesthesia),¹³ hypercarbia and hypoxia.¹⁴ Arrhythmogenic mechanisms of succinylcholine include acute hyperkalaemia and modulation of sympathetic outflow through actions on pre- and post-synaptic nicotinic and muscarinic receptors.^{15,16} Empiric observation also strongly support an increased propensity to succinylcholine-induced bradycardia in infants¹ and following repeated doses.⁴

Atropine^{5,6,17} and glycopyrrolate^{6,17} reduce the inci-

TABLE III Heart rate (beats $\cdot$ min⁻¹)

Group	Pre-induction	Post-induction	1 min post-laryngoscopy	3 min post-laryngoscopy
S/A 10	101.3 (25.1)	120.8 (27.1)	128.3 (23)	127.2 (19.3)
S/A 20	107.5 (26.5)	134.2 (25.5)	144.5 (18.9)	139.5 (20.2)
Vecuronium	102.5 (25.3)	105.9 (17.5)	120.4 (16.3)	120.2 (21.1)

Mean $\pm$ (SD); S/A; 10: succinylcholine/atropine ($10 \mu\text{g} \cdot \text{kg}^{-1}$); S/A 20: succinylcholine/atropine ($20 \mu\text{g} \cdot \text{kg}^{-1}$).

TABLE IV Changes in heart rate and mean arterial pressure following study drug combinations and laryngoscopy/intubation

Group	S/A 10 (n = 12)	S/A 20 (n = 13)	Vec (n = 11)
D (1) MAP	21.1 (17.7)	10.2 (15.0)	-1.8 (17.5)
D (1) HR	18.4 (12.2)*	25.1 (15.2)*	3.5 (20.7)
D (2) MAP	22.6 (12.8)	26.0 (22.2)	23.2 (15.6)
D (2) HR	31.3 (22.0)	38.1 (23.6)	24.3 (35.6)

Mean $\pm$ (SD); D (1) represents greatest change from pre-induction to pre-laryngoscopy; D (2) represents greatest change from pre-induction to post-laryngoscopy.

* $P < 0.05$ compared to vecuronium.

dence of succinylcholine-induced bradycardia in both children and adults. The doses of atropine found to be effective for this purpose were $9 \mu\text{g} \cdot \text{kg}^{-1}$ (adults), $20 \mu\text{g} \cdot \text{kg}^{-1}$ (children aged 1–7 yr) and $10 \mu\text{g} \cdot \text{kg}^{-1}$ (infants). No dose response study has been performed in any group.

Thiopentone has been shown in animal experiments to potentiate the arrhythmogenic effects of epinephrine.^{18–21} Increasing thiopentone concentrations produces a dose-dependant reduction in the arrhythmogenic dose of epinephrine in dogs.¹⁸ We consider it unlikely that this thiopentone effect influenced our results because (1) a low incidence of arrhythmias (6%) occurred, (2) those observed were atrial and not the typical ventricular arrhythmias caused by catecholamines, (3) all three study groups received thiopentone. However, there is also substantial clinical evidence to indicate that thiopentone reduces the incidence of succinylcholine-induced bradycardia in adults and children.^{22,23} The absence of succinylcholine-induced bradycardia in this study may be attributable either to the prior administration of either dose of atropine or to the use of thiopentone. Because administration of succinylcholine without administration of an antimuscarinic agent is not accepted practice in this institution, the relative importance of these two protective factors was not determined.

A multitude of factors can alter haemodynamic variables around the time of induction of anaesthesia. For this reason, we included for comparison a group which

received vecuronium, a non-depolarizing muscle relaxant of well-established cardiovascular stability in children.^{7,8} Although the mean increases in heart rate and mean arterial pressure following vecuronium were less than those in either of the succinylcholine/atropine groups, there was marked variation in the responses seen in all three groups. This may be due to the variable degree of preoperative anxiety present in these unpremedicated children.

The haemodynamic responses to atropine $10 \mu\text{g} \cdot \text{kg}^{-1}$ or $20 \mu\text{g} \cdot \text{kg}^{-1}$ prior to the administration of succinylcholine $1.5 \text{ mg} \cdot \text{kg}^{-1}$ in older children anaesthetized with thiopentone are similar. Succinylcholine-induced bradycardia was not observed in any patient who received either dose of atropine. The changes in heart rate and mean arterial pressure to vecuronium in this population was less than that following either dose of atropine, but demonstrated marked interpatient variability. In conclusion, under the study conditions described, atropine $20 \mu\text{g} \cdot \text{kg}^{-1}$ offers no advantage over atropine $10 \mu\text{g} \cdot \text{kg}^{-1}$ when administered before succinylcholine in older children.

References

- 1 Leigh MD, McCoy DD, Belton KM, Lewis GB. Bradycardia following intravenous administration of succinylcholine chloride to infants and children. *Anesthesiology* 1957; 18: 698–702.
- 2 Craythorne NWB, Turndorf H, Dripps RD. Changes in pulse rate and rhythm associated with the use of succinylcholine in anesthetized patients. *Anesthesiology* 1960; 21: 465–70.
- 3 Lupprian KG, Churchill-Davidson HC. Effect of suxamethonium on cardiac rhythm. *BMJ* 1960; 2: 1774–7.
- 4 Williams CH, Deutsch S, Linde HW, Bullough JW, Dripps RD. Effects of intravenously administered succinylcholine on cardiac rate, rhythm, and arterial blood pressure in anesthetized man. *Anesthesiology* 1961; 22: 947–54.
- 5 Lerman J, Chinyanga HM. The heart rate response to succinylcholine in children: a comparison of atropine and glycopyrrolate. *Can Anaesth Soc J* 1983; 30: 377–81.
- 6 Goudsouzian NG. Turbe del ritmo cardiaco durante intubazione tracheale nei bambini. *Acta Anesthesiologica Italica* 1981; 32: 293–6.
- 7 Ferres CJ, Crean PM, Mirakhur RK. An evaluation of ORG NC 45 (vecuronium) in paediatric anaesthesia. *Anaesthesia* 1983; 38: 943–7.
- 8 Goudsouzian NG, Martyn JJA, Liu LMP, Gionfriddo M. Safety and efficacy of vecuronium in adolescents and children. *Anesth Analg* 1983; 62: 1083–8.
- 9 Barreto RS. Effect of intravenously administered succinylcholine upon cardiac rate and rhythm. *Anesthesiology* 1960; 21: 401–4.
- 10 Pérez HR. Cardiac arrhythmias after succinylcholine. *Anesth Analg* 1970; 49: 33–7.
- 11 Delphin E, Jackson D, Rothstein P. Use of succinylcholine during elective pediatric anesthesia should be reevaluated. *Anesth Analg* 1987; 66: 1190–2.
- 12 Katz RL, Epstein RA. The interaction of anesthetic agents and adrenergic drugs to produce cardiac arrhythmias. *Anesthesiology* 1968; 29: 763–9.
- 13 Gibbs JM. The effects of endotracheal intubation on cardiac rate and rhythm. *NZ Med J* 1967; 66: 465–9.
- 14 Davis RF. Etiology and treatment of perioperative cardiac arrhythmias. In: Kaplan JA (Ed.). *Cardiac Anesthesia*, 3rd ed. Philadelphia: W.B. Saunders Co. 1993; 179.
- 15 Nigrovic V. Succinylcholine, cholinergic receptors and catecholamines: proposed mechanism of early adverse haemodynamic reactions. *Can Anaesth Soc J* 1984; 31: 382–94.
- 16 Leiman BC, Katz J, Butler BD. Mechanisms of succinylcholine-induced arrhythmias in hypoxic or hypercarbic dogs. *Anesth Analg* 1987; 66: 1292–7.
- 17 Sørensen O, Eriksen S, Hommelgaard P, Viby-Mogensen J. Thiopental-nitrous oxide-halothane anesthesia and repeated succinylcholine: comparison of preoperative glycopyrrolate and atropine administration. *Anesth Analg* 1980; 59: 686–9.
- 18 Hayashi Y, Sumikawa K, Yamatodani A, Tashiro C, Wada H, Yoshiya I. Myocardial sensitization by thiopental to arrhythmogenic action of epinephrine in dogs. *Anesthesiology* 1989; 71: 929–35.
- 19 Lina AE, Dauchot PJ, Anton AH. Epinephrine-aminophylline-induced arrhythmias after midazolam or thiopentone in halothane-anaesthetized dogs. *Can J Anaesth* 1991; 28: 1037–42.
- 20 Atlee JL III, Malkinson CE. Potentiation by thiopental of halothane-epinephrine-induced arrhythmias in dogs. *Anesthesiology* 1982; 57: 285–8.
- 21 Bednarski RM, Majors LJ, Atlee JL. Epinephrine-induced ventricular arrhythmias in dogs anesthetized with halothane: potentiation by thiopental and thiopental. *Am J Vet Res* 1985; 46: 1829–31.
- 22 Schoenstadt DA, Whitcher CE. Observations on the mechanism of succinylcholine-induced cardiac arrhythmias. *Anesthesiology* 1963; 24: 358–62.
- 23 Badgwell JM, Cunliffe M, Lerman J. Thiopental attenuates dysrhythmias in children: comparison of induction regimens. *Texas Med* 1990; 86: 36–8.