Should the routine use of atropine before succinylcholine in children be reconsidered?

Georgina McAuliffe MB BS FRCA,
Bruno Bissonnette MD FRCPC,
Christine Boutin MD FRCPC*

It is common practice to administer atropine before a first dose of succinylcholine in infants and children. However, the administration of succinylcholine without atropine has not been investigated in children. This study was designed to compare cardiovascular changes after the administration of either atropine with succinylcholine or succinylcholine alone. In 41 ASA I or II patients aged from 1 to 12 yr anaesthesia was induced with thiopentone 5 mg · kg^{-1}. Patients were randomly allocated to receive either atropine 20 μg · kg^{-1} and succinylcholine 1.5 mg · kg^{-1} (n = 20) or succinylcholine 1.5 mg · kg^{-1} alone (n = 21). Heart rate and rhythm were recorded continuously from two minutes before induction until two minutes after tracheal intubation. Blood pressure was measured non-invasively before and after induction of anaesthesia and both immediately and two minutes after laryngoscopy. One self-limiting episode of bradycardia was recorded during laryngoscopy in a child who received atropine. Heart rate increased in both groups compared with baseline values (108 ± 25), with a greater increase in patients who had received atropine (150 ± 13) than in those who had not (128 ± 18) (P < 0.05). There was no difference in mean arterial pressure or incidence of arrythmias between the two groups. No recorded arrythmias were judged to be clinically important by a cardiologist. The incidence of bradycardia after succinylcholine in the absence of atropine in children aged from 1 to 12 yr appears to be lower than previously estimated. The use of atropine before a single dose of succinylcholine in children deserves to be reconsidered.

Key words
ANAESTHESIA: paediatric;
HEART: arrythmia; bradycardia;
NEUROMUSCULAR RELAXANTS: succinylcholine;
PARASYMPATHETIC NERVOUS SYSTEM: atropine.

From the Departments of Anaesthesia and Cardiology*, 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, Ontario, Canada. M5G 1X8.

Accepted for publication 4th April, 1995.

On administre d'habitude de l'atropine avant la succinylcholine aux nourrissons et aux enfants. Toutefois, l'administration de succinylcholine sans atropine n'a jamais été étudiée chez ces enfants. Cette étude a été planifiée pour comparer les changements cardiovasculaires survenant après l'administration soit d'atropine et de succinylcholine soit de succinylcholine seulement. L'anesthésie de 41 enfants ASA I et II âgés de 1 à 12 ans a été induite avec du thiopentone 5 mg · kg^{-1}. Les enfants ont été répartis au hasard de façon à recevoir soit de l'atropine 20 μg · kg^{-1} avec succinylcholine 1,5 mg · kg^{-1} (n = 20) soit de la succinylcholine 1,5 mg · kg^{-1} seulement (n = 21). La fréquence et le rythme cardiaque sont enregistrés continuellement deux minutes avant l'induction jusqu'à deux minutes après l'intubation de la trachée. La pression artérielle est mesurée par la méthode non effractive avant et après l'induction de l'anesthésie et immédiatement après la laryngoscopie et deux minutes plus tard. Un épisode de bradycardie est enregistré pendant la laryngoscopie chez un enfant qui a reçu de l'atropine. Comparativement aux valeurs initiales, la fréquence cardiaque augmente dans les deux groupes (108 ± 25), avec une augmentation plus importante chez ceux qui ont reçu l'atropine (150 ± 13) que chez ceux qui ne l'ont pas reçue (128 ± 18) (P < 0,05). On ne note pas de différence pour ce qui est de la pression artérielle moyenne ou de l'incidence des arythmies entre les deux groupes. Aucune des arythmies enregistrées n'a été jugée importante par un cardiologiste. En absence d'atropine, l'incidence de la bradycardie après la succinylcholine chez des enfants âgés de 1 à 12 ans semble plus basse qu'on l'estimait auparavant. L'utilisation d'atropine avant une dose unique de succinylcholine mérite d'être revue.

The risk of sinus bradycardia in infants and children following a single dose of succinylcholine was first described over 30 yr ago.[1] In children aged from one to seven years atropine 20 μg · kg^{-1} is thought to prevent bradycardia following the administration of succinylcholine.[2] In infants, the administration of atropine 10 μg · kg^{-1} reduces but does not eliminate the incidence of arrythmias following administration of succinylcholine.[3] Shorten *et al.*[4] were unable to demonstrate any differences in cardiovascular stability after succinylcholine administration in

children aged from six to twelve years who had received either 10 or 20 $\mu g \cdot kg^{-1}$ of atropine. Therefore, the role of routine prophylactic atropine in maintaining cardiovascular stability when given before succinylcholine in children remains unclear.

The use of atropine in neonates, infants and children varies widely. In a survey on the use of atropine by Australian anaesthetists 86% of all fellows of the Australian and New Zealand College of Anaesthetists replied to a questionnaire on their use of prophylactic atropine.[5] Less than half the respondents gave atropine to children over the age of one year before a first dose of succinylcholine. The only indication for which a convincing majority of anaesthetists agreed that a prophylactic dose of atropine should be given was prior to a repeated dose of succinylcholine. Recently Warde *et al.* reported results of a survey of 1369 members of the Society for Paediatric Anesthesia and the Association of Paediatric Anaesthetists of Great Britain and Ireland (65.5% response rate).[6] Less than half of the respondents routinely use anticholinergics even in children less than one year of age. The overall pattern of practice appeared similar in both North America and the United Kingdom.

The objective of this study was to compare the changes in heart rate, rhythm and mean arterial pressure following administration of either atropine 20 $\mu g \cdot kg^{-1}$ with succinylcholine 1.5 $\mu g \cdot kg^{-1}$ or succinylcholine 1.5 $\mu g \cdot kg^{-1}$ alone to children aged from one to twelve years following induction of anaesthesia with thiopentone.

Methods

After obtaining approval from the Human Subject Review Committee and written informed parental consent, 41 ASA I or II children aged from one to twelve years undergoing elective surgical procedures for which tracheal intubation was indicated were studied. Patients were excluded if a history of neuromuscular disease, malignant hyperthermia 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 monitoring was applied and a record of two minutes continuous ECG monitoring (lead II) was obtained. The insertion of a 22 G intravenous cannula was facilitated by 66% nitrous oxide in oxygen administered by facemask.

The study period extended from two minutes before induction of anaesthesia until two minutes after tracheal intubation. During this time, heart rate and rhythm (lead II) were monitored continuously. Blood pressure was monitored non-invasively with a Datex AS/3 (Datex Instrumentarium Corporation, Helsinki, Finland) immediately before induction of anaesthesia, after induction but before laryngoscopy, immediately after laryngoscopy and two minutes after laryngoscopy.

Anaesthesia was induced with thiopentone 5 $mg \cdot kg^{-1}$. Patients were randomly allocated to one of two groups: Group AS received atropine 20 $\mu g \cdot kg^{-1}$ immediately followed by succinylcholine 1.5 $mg \cdot kg^{-1}$ and Group S received succinylcholine 1.5 $mg \cdot kg^{-1}$ alone after the loss of the lash reflex to facilitate tracheal intubation. These drugs were administered by rapid bolus injection followed by a flush of 5 ml normal saline. Manual intermittent positive-pressure ventilation with nitrous oxide 66% in oxygen was instituted to maintain $SpO_2 > 97\%$ and $PETCO_2$ within normal limits (35–45 mmHg) using the Jackson Rees modification of Ayre's T-piece or a circle system for children over 20 kg. Thirty to forty-five seconds after the completion of the injection of succinylcholine, and after a post-induction blood pressure was obtained, direct laryngoscopy and tracheal intubation were performed. Anaesthesia was maintained after laryngoscopy by intermittent postive-pressure ventilation using nitrous oxide 66% in oxygen and halothane 1.5% until spontaneous ventilation commenced.

Each ECG tracing was examined by a cardiologist who identifed the presence and nature of arrhythmias. This physician was unaware of the study group to which the ECG belonged. For the purpose of the study, bradycardia was defined as three or more beats at a rate of less than 60 beats $\cdot min^{-1}$ or a 20% reduction in heart rate from the pre-induction rate in association with a decrease in mean arterial pressure of over 20%. It was decided that if such a bradycardia were to be observed, then atropine 20 $\mu g \cdot kg^{-1}$ *iv* would be administered.

Statistical analysis

All data with parametric values are reported as mean $\pm$ standard deviation. The sample size was calculated for a power of 90% with $\alpha = 0.05$ using an incidence of succinylcholine-induced bradycardia of 50%,[2,11] reducing to 0% after the administration of atropine.[3] Unpaired Student's t test was used to analyse data between groups at corresponding study periods whereas within group data analysis was performed using repeated measures ANOVA and Dunnett's q statistic for multiple comparison testing against the control mean. Data with non-parametric values were analysed using Fisher's exact test. $P < 0.05$ was accepted as statistically significant.

Results

Demographic data are reported in Table I and are similar in the two groups.

The changes in heart rate and mean arterial pressure are summarised in Tables II and III. In both groups the heart rate increased from pre-induction values ($P <$

TABLE I Demographic data

Group	*Age (yr)*	*Sex (M:F)*	*Weight (kg)*
AS ($n = 20$)	5.7 ± 2.7	8:12	21.6 ± 8.4
S ($n = 21$)	5.1 ± 3.1	8:13	21.5 ± 10.3

Mean ± SD.
A/S: atropine/succinylcholine; S: succinylcholine.

TABLE II Heart rate (beats · min^{-1})

	Heart rate		
Time	*Group S*	*Group AS*	**P < 0.05*
Pre-induction	108 ± 25 (70–165)	108 ± 17 (83–140)	NS
Pre-laryngoscopy	128 ± 24† (95–160)	142 ± 15† (116–169)	*
Post-laryngoscopy	128 ± 18† (92–157)	150 ± 13† (116–168)	*
2 mins post-laryngoscopy	117 ± 18† (78–146)	149 ± 12† (123–165)	*

Mean ± SD; (range); NS = not significant;
AS = atropine/succinylcholine: S = succinylcholine alone.
†$P < 0.05$ compared with pre-induction value.

TABLE III Mean arterial pressure (mmHg)

	Mean arterial pressure		
Time	*Group S*	*Group AS*	**P < 0.05*
Pre-induction	94 ± 13 (80–130)	90 ± 11 (72–114)	NS
Post-induction/pre-laryngoscopy	100 ± 16 (64–130)	101 ± 15† (65–129)	NS
Post-laryngoscopy	107 ± 15† (81–130)	110 ± 18† (75–158)	NS
2 min post-laryngoscopy	86 ± 12† (68–116)	89 ± 11 (74–116)	NS

Mean ± SD; (range); NS = not significant;
A/S = atropine/succinylcholine: S = succinylcholine alone.
†$P < 0.05$ compared with preinduction value.

0.05). The magnitude of the increase in heart rate was greater in those who had received atropine than in those who had received succinylcholine alone ($P < 0.05$). The mean arterial pressure increased in each group after laryngoscopy compared with pre-induction values ($P < 0.05$) and then returned two minutes after laryngoscopy to levels similar to or slightly lower than pre-induction. There were no differences in mean arterial pressure between the groups at any time.

There was one episode of bradycardia in a three-year-old child who had received atropine. This child had a pre-induction rhythm disturbance of ectopic atrial activity. During laryngoscopy he had a 2.8 sec sinus pause followed by a slow junctional and slow atrial escape rhythm. The rhythm reverted spontaneously to sinus rhythm with its original ectopic atrial activity. Overall, three patients who had received succinylcholine alone and seven patients who had received atropine with succinylcholine had minor arrythmias none of which were judged to be clinically important by the cardiologist (Table IV). The difference in the incidence of arrythmias between the groups was not statistically significant. No patient required treatment of bradycardia and there were no other complications throughout the study.

TABLE IV Changes in rhythm during the study

Patient treatment number	*Period 1*	*Period 2*	*Period 3*
Group S			
No. 7	SR	VC	PVC, VC
No. 9	SR	SR	PAC
No. 18	SR	SR	J
Group SA			
No. 4	PAC	SR	SR
No. 8	SR	PVC	PVC
No. 10	SR	Sinus Pause	SR
No. 20	PAC	SR	SR
No. 26	EAActivity	Sinus Pause	EAActivity
No. 31		Bradycardia, JE, AE	
No. 38	SR	SR	PVC
No. 40	SR	SR	PVC, VC

Period 1: Preinduction to laryngoscopy, Period 2: Laryngoscopy, Period 3: Post-laryngoscopy, SR: sinus rhythm, VC: ventricular couplets, PVC: premature ventricular contraction, PAC: premature atrial contraction, EAActivity: ectopic atrial activity, J: junctional, JE: junctional escape, AE: atrial escape.

Discussion

The data reported in this study indicate that the incidence of succinylcholine-induced bradycardia in children aged from one to twelve years is lower than previously thought. The administration of prophylactic atropine with succinylcholine magnified the increase in heart rate that is observed without its use but had no effect on mean arterial pressure. Transient bradycardia was observed during laryngoscopy in one patient who had received 20 $\mu g \cdot kg^{-1}$ atropine and had pre-existing atrial ectopic activity before induction.

There are many reports of cardiac arrythmias following the administration of succinylcholine to normal children including sinus bradycardia,[7] sinus tachycardia,[7,8] ventricular ectopics[8] and ventricular bigeminy[8] but a causal relationship between the arrythmias and succinylcholine

has never been clear. Empirical observation supports an increased propensity to bradycardia in infants[2] and after repeated doses of succinylcholine.[9] Proposed arrythmogenic mechanisms of succinylcholine-induced arrhythmias include acute hyperkalaemia and modulation of parasympathethic outflow through actions on pre- and post-synaptic nicotinic and muscarinic receptors.[10,11]

In 1957 Leigh first reported the occurrence of succinylcholine-induced bradycardia in children.[1] His patients received scopolamine premedication combined with a variety of anaesthetic techniques. He described four cases "representative of the series" of 23 patients of whom three out of four developed bradycardia after succinylcholine. The heart rates varied from 50 to 100 beats · min^{-1}. Review of the literature reveals that there are no randomised controlled trials comparing incidences of succinylcholine-induced bradycardia in children with and without the use of anticholinergic medication. In 1960, however, Craythorne observed an incidence of succinylcholine-induced bradycardia in unpremedicated children aged from four months to five years in three out of four cases.[12] These three children all had nodal rhythms with minimum heart rates of 41, 54 and 79 beats · min^{-1} respectively. In children who had received scopolamine premedication (aged from 2–6 yr) five of eighteen cases (28%) developed bradycardia as defined by a decrease in heart rate of >20% from pre-induction rates with minimum heart rates ranging from sinus arrest to 72 beats · min^{-1}.

The original reports of succinylcholine-induced bradycardia in children were published at a time when a variety of non-standardised and now superseded premedicant and anaesthetic drugs were used.[2,7,8,12,13] These included heavy sedative premedication which may have predisposed the children to unrecognised hypoxia and frequent use of cyclopropane which is a particularly arrythmogenic agent. Other factors which may have increased the incidence of arrythmias included the combination of halogenated hydrocarbon volatile agents with circulating catecholamines,[14] laryngoscopy and intubation in the presence of "light" anaesthesia,[15] hypercarbia and hypoxia.[16] Routine monitoring of end-tidal gas levels was unavailable at this time and as Barreto indicated in 1960, the only way to determine the role of hypoxia in arrythmias was to measure arterial oxygen saturation which was not routinely performed.[7] Previous studies have also varied in their definitions of bradycardia.[2,3,12]

The low incidence of succinylcholine-induced bradycardia in this study may be attributable to several factors. Firstly, the oxygen saturation and the end-tidal carbon dioxide were maintained within normal limits. Secondly, it has been suggested that a deep level of anaesthesia and the use of thiopentone may protect against bradycardia induced by succinylcholine.[17,18] Thirdly, the children may have been in a light plane of anaesthesia which could have protected against bradycardia. The contribution of older anaesthetic agents on the incidence of bradycardia has been discussed earlier. Lastly, the children in this study were unpremedicated. One could therefore postulate that they might have had high levels of circulating catecholamines released due to anxiety which may have offered protection against bradycardia.

Despite atropine prophylaxis one patient developed bradycardia during intubation. The explanation for this is not clear although his underlying rhythm disturbance may have predisposed him to perioperative arrythmias particularly if combined with a relatively light plane of anaesthesia and a potent vagal stimulus such as tracheal intubation. Atropine itself has a complex effect on heart rate and the response of the SA node is bimodal, slowing with small doses and accelerating with larger doses.[19] Therefore it is possible that this was an idiosyncratic response to atropine despite an appropriate dose. It is also possible that the bradycardia would have been more prolonged had the child not received atropine.

The use of atropine in adults as prophylaxis against bradycardia and for its antisialogogue properties has declined over the last 20 years and many anaesthetists feel that its use is unnecessary and often inadvisable.[20] The use of atropine in adults receiving thiopentone and succinylcholine has been shown to be associated with an increased incidence of arrythmias at induction.[21,22] Although bradycardia has been described in healthy adults after a single dose of succinylcholine, particularly when fentanyl and droperidol have been included as part of the induction technique, these episodes have never been associated with any long-term clinical morbidity.[23,24] Atropine has a number of side effects which may dissuade anaesthetists from its use including tachycardia, dry mouth, flushing and visual blurring.[25] It is associated with arrythmias including A-V dissociation, A-V block, nodal rhythm and ventricular extrasystole.[26] Sweating is suppressed and a rise in body temperature may occur. There are also central nervous system effects of drowsiness, restlessness and confusion. In addition, the tachycardia caused by atropine obscures the normal pulse rate which is a valuable sign used in assessing depth of anaesthesia, volume status and hypoxia.

In paediatric practice many anaesthetists continue to recommend the use of atropine before anaesthesia in the belief that it prevents bradycardia that may occur due to mechanical stimulation, succinylcholine, halothane or powerful reflexes such as the oculocardiac reflex.[22,27–30] The importance of avoiding bradycardia in neonates has been emphasised because their cardiac output is considered to be predominantly heart rate dependent in the

presence of immature contractility and reduced ventricular compliance.[31-33] However, it has never been established at what age cardiac output becomes predominantly stroke volume dependent, what the "optimum" heart rate for maximum cardiac output is at any age or what cardiac output is desirable in anaesthetised children.

The use of succinylcholine in children has been under recent debate and review because of its rare association with hyperkalaemic arrest in children with undiagnosed myopathies. This led Burroughs-Wellcome to issue a controversial drug label contraindication statement that has subsequently been reduced to a warning. The warning states that "in infants and children, especially in boys under eight years of age, the rare possibility of inducing life-threatening hyperkalaemia in undiagnosed myopathies by the use of succinylcholine must be balanced against the risk of alternative means of securing the airway." Some authors have advocated re-evaluating the use of succinylcholine for elective anaesthesia[34] whilst others have stressed its long history of safe usage and feel that hyperkalaemic arrest is treatable provided that a prompt diagnosis is made.[35,36] In addition, it is not clear how morbidity would be affected if succinylcholine was to be abandoned for elective cases in favour of the non-depolarizing agents.

Succinylcholine remains unique in its ability to provide profound neuromuscular blockade of rapid onset and offset and it seems likely that even if its elective use is declining its vital role in patients at risk of pulmonary aspiration will continue until a reliable and safe alternative is found. Succinylcholine-induced side effects are therefore still relevant to anaesthetists dealing with the paediatric population.

The unexpectedly low incidence (0%) of bradycardia has rendered the power of this study insufficient to infer that there is no difference in the incidence of succinylcholine-induced bradycardia with and without atropine. A zero incidence of bradycardia in a sample of 20 patients means that at the upper 95% confidence limit the true incidence of bradycardia could still be as high as 15%.[37] This incidence is considerably lower than previous reports suggested and possible explanations for this have already been described. The true incidence and clinical relevance of succinylcholine-induced bradycardia in children remains unclear. Its elucidation will require the study of a larger sample of patients. It is also possible that a larger study would confirm the trend we observed of an increased incidence of minor arrythmias after the use of atropine.

In conclusion, this study suggests that the routine use of atropine before succinylcholine in children aged from one to twelve years needs to be reconsidered. Until the true risks and benefits of atropine usage before succinylcholine are established we are unable to recommend that anaesthetists change their current practice at this time, whether or not this includes routine use of prophylactic atropine.

Acknowledgment

The authors would like to thank Dr. J.E.S. Relton for his help in the preparation of the manuscript.

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