EFFECT OF ATROPINE ON BRADYDYSRHYTHMIAS INDUCED BY SUCCINYLCHOLINE FOLLOWING PRETREATMENT WITH D-TUBOCURARINE

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ABSTRACT

This study was designed to compare the effectiveness of pretreatment with the combination of d-tubocurarine and atropine with d-tubocurarine alone in preventing changes in cardiac rate and rhythm following repeated administration of succinylcholine. Sixty subjects were randomly divided into three groups of twenty. Group one received d-tubocurarine $0.04 \text{ mg} \cdot \text{kg}^{-1}$ and atropine $0.01 \text{ mg} \cdot \text{kg}^{-1}$, and group two d-tubocurarine $0.04 \text{ mg} \cdot \text{kg}^{-1}$ only, given three minutes before induction of anaesthesia. Group three received no pretreatment. Immediately following thiopentone induction succinylcholine $1 \text{ mg} \cdot \text{kg}^{-1}$ was given to all patients. A further dose of succinylcholine $1 \text{ mg} \cdot \text{kg}^{-1}$ was given to patients in the pretreatment groups following recovery of neuro-muscular function. Both pretreatment groups showed a small statistically significant fall in mean heart rate after the second dose of succinylcholine. One patient in each pretreatment group showed a fall in heart rate to less than $50 \text{ beats min}^{-1}$; two patients in the group who received both d-tubocurarine and atropine, and three patients in the d-tubocurarine only group, showed a fall in heart rate of 25 per cent or more. It is concluded that the addition of atropine may be unnecessary for prevention of succinylcholine-induced bradydysrhythmias when d-tubocurarine pretreatment is given.

KEY WORDS: NEUROMUSCULAR RELAXANTS, succinylcholine, d-tubocurarine; ANTICHOLINERGICS, atropine; COMPLICATIONS, bradydysrhythmia.

SEVERE BRADYCARDIA may follow repeated administration of succinylcholine if no protective pretreatment is given.^{1,2} Pretreatment with small doses of non-depolarizing relaxants when anticholinergic drugs have also been administered has been shown to diminish the incidence of such bradycardia.^{3,4} Atropine alone, even administered in large doses, may not be effective against succinylcholine-induced bradycardias.⁵ The addition of atropine does not affect the protection against bradycardias afforded by gallamine pretreatment,⁶ but gallamine even in small pretreatment doses causes significant tachycardia. Non-depolarizing relaxants which do not cause tachycardia have not been studied with reference to concomitant anticholinergic administration. The purpose of this study was to compare the effectiveness of pretreatment with d-tubocurarine alone and in combination with

atropine on the bradydysrhythmias consequent on repeated administration of succinylcholine.

METHODS

Sixty patients of ASA class I presenting for routine gynaecological operations were studied. All patients were visited preoperatively by one of us, and informed consent was obtained. The procedure was approved by the hospital ethical committee. Premedication consisted of an intramuscular injection of meperidine 50 mg and promethazine 25 mg one hour before operation. The patients were randomly allocated to three groups, with twenty patients in each group.

Patients in the first group were pretreated with d-tubocurarine $0.04 \text{ mg} \cdot \text{kg}^{-1}$ intravenously⁷ three minutes before induction, while those in the second group received both d-tubocurarine $0.04 \text{ mg} \cdot \text{kg}^{-1}$ and atropine $0.01 \text{ mg} \cdot \text{kg}^{-1}$.⁶ Patients in the third group did not receive pretreatment (Figure 1).

Anaesthesia was induced with a sleep dose of thiopentone which amounted to $4 \text{ mg} \cdot \text{kg}^{-1}$ and this was followed immediately by succinylcholine $1 \text{ mg} \cdot \text{kg}^{-1}$. The patients were ventilated with nitrous oxide 70 per cent with oxygen. Tracheal

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FIGURE 1 Time sequence of anaesthesia and administration of drugs. — indicates range of times.

intubation was not attempted, nor did the operation commence during the study period. Neuromuscular blockade was monitored with a peripheral nerve stimulator, using single twitches at ten second intervals, and when neuromuscular transmission returned to pre-succinylcholine levels a second dose of succinylcholine $1 \text{ mg} \cdot \text{kg}^{-1}$ was administered to patients in the two pretreatment groups. The time interval between doses was from four to five minutes in all cases. It was felt to be ethically unjustifiable to repeat the succinylcholine dose in the control group who were not pretreated in view of the severe bradycardias which have been demonstrated to occur.⁸

Throughout the study period the electrocardiogram was monitored using a Tektronix model 414 monitor with a paper readout which was analyzed postoperatively by one of the authors who was not involved with the anaesthetic and who did not know the anaesthetic technique used.

All patients had normal preoperative serum potassium levels. An arterial blood sample was taken immediately after the intubating dose of succinylcholine and again after the subsequent dose, and Paco_2 was measured with a Corning model 165 blood gas analyzer. In order to exclude changes in cardiac rate and rhythm caused by gross alterations in Paco_2 , it was decided that a range of Paco_2 between 3.3 and 6.7 kPa (25 and 50 mm Hg) would be acceptable,⁶ and all patients fell within these limits.

The data were analyzed by student's *t* test and χ^2 test where appropriate.

RESULTS

The mean heart rates throughout the study are shown in Figure 2. There was no statistical difference between the mean heart rates of the three groups before pretreatment. The mean heart rate was significantly higher before induction ($P < 0.01$) in the group which had received atropine pretreatment (Figure 2).

Figure 3 shows the maximum changes in heart rate and also changes in rhythm from one minute

FIGURE 2 Mean heart rates $\pm$ S.E.M. during the observation period. ○—○ atropine and d-tubocurarine pretreatment. ●—● d-tubocurarine only pretreatment. □—□ control group.

FIGURE 3 Maximum changes in cardiac rate in pretreated groups after second injection of succinylcholine, and in control group over same period.

before administration of the second dose of succinylcholine to one minute after. When compared to the mean pre-succinylcholine heart rate, there was a small statistically significant fall ($P < 0.05$) in mean heart rate in both pretreatment groups, while no change occurred in the control group over the same period. One patient in each pretreatment group showed a transient decrease in heart rate to less than 50 beats min^{-1} , the patient in the d-tubocurarine only group showing nodal rhythm. Three patients in the d-tubocurarine only pretreatment group and two patients in the d-tubocurarine and atropine group showed a decrease in heart rate of 25 per cent or more from pre-succinylcholine levels. These differences were not statistically significant (χ^2 test). The group who received atropine and d-tubocurarine pretreatment continued to show a significantly higher mean heart rate (*t* test $P < 0.05$) at all times during the observation period.

DISCUSSION

The occurrence of bradycardia following repeated administration of succinylcholine is

affected by many factors. Thiopentone induction protects against severe changes in cardiac rhythm following succinylcholine,⁹ probably due to its vagolytic properties.¹⁰ Halothane may sensitize the heart to such effects when used as an induction agent and, especially, after prolonged administration.² When halothane is used as an induction agent neither atropine, unless given in large doses causing considerable tachycardia, nor gallamine protects against serious bradydysrhythmias caused by a second dose of succinylcholine.^{5,10} Other authors have shown that atropine given intravenously, but not intramuscularly, may protect against bradycardia following repeated doses of succinylcholine.² Timing of the second injection of succinylcholine is also important, maximum bradycardia occurring when the second dose is given five minutes after the first.³ Absence of other stimulation, such as intubation or surgical intervention, increases the frequency and degree of bradycardia.⁵ The protective effect of pretreatment with gallamine against bradydysrhythmia is not altered by the addition of atropine pretreatment.⁶ Gallamine, when administered both in paralyzing and in small pretreatment doses causes significant tachycardia,^{6,12} and this effect makes the additional value of atropine difficult to assess. Our results from a small number of subjects indicate that pre-operative intravenous administration of atropine may not increase the protective effect of pretreatment with d-tubocurarine against bradydysrhythmia consequent on a second dose of succinylcholine. Atropine also causes a possibly dangerous increase in heart rate⁵ and may cause various forms of dysrhythmia when administered intravenously.¹³ We conclude, therefore, that the addition of atropine may be unnecessary with respect to prevention of bradydysrhythmia when d-tubocurarine is used as pretreatment.

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RÉSUMÉ

L'efficacité d'une injection d'atropine et de d-tubocurarine précédant l'administration de doses répétées de succinylcholine, en vue de prévenir les modifications de fréquence et de rythme observées dans ces cas, a été comparée à la valeur préventive d'une injection de d-tubocurarine employée seule. L'étude a été conduite chez soixante patients assignés à l'un des trois groupes de vingt patients.

Les patients du groupe I ont reçu, juste avant l'induction de l'anesthésie, une injection de d-tubocurarine $0.04 \text{ mg} \cdot \text{kg}^{-1}$ et d'atropine $0.01 \text{ mg} \cdot \text{kg}^{-1}$; ceux du groupe II n'ont reçu que la d-tubocurarine (la même dose) avant l'induction; ceux du groupe III n'ont pas reçu de pré-traitement. Une dose de succinylcholine à raison de $1 \text{ mg} \cdot \text{kg}^{-1}$ était administrée à tous les patients immédiatement après l'induction. Puis dès le retour de la fonction neuro-musculaire, on répétait la même dose de succinylcholine aux patients des groupes I et II. Une diminution légère mais significative de la fréquence cardiaque moyenne a été observée après la seconde injection de succinylcholine chez les patients de ces deux groupes. Une fréquence inférieure à 50/minute a été notée chez l'un des patients des groupes I et II; deux patients du groupe I (d-tubocurarine et atropine) et trois du groupe II (d-tubocurarine seule) ont présenté une fréquence cardiaque abaissée de 25 pour cent ou plus.

En conclusion, l'addition d'atropine ne semble pas nécessaire pour prévenir les bradyarythmies associées à l'administration de doses répétées de succinylcholine lorsque les malades reçoivent un pré-traitement à la d-tubocurarine.