CARDIAC EFFECTS OF ATROPINE AND GALLAMINE IN PATIENTS RECEIVING SUXAMETHONIUM

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Eighty healthy patients were randomly allocated to four groups. Atropine 0.01 mg kg$^{-1}$ i.v. (group I), gallamine 0.3 mg kg$^{-1}$ i.v. (group II), atropine 0.01 mg kg$^{-1}$ i.m. and gallamine 0.3 mg kg$^{-1}$ i.v. (group III), or atropine 0.01 mg kg$^{-1}$ i.v. and gallamine 0.3 mg kg$^{-1}$ i.v. (group IV) were given before operation. After induction of anaesthesia with thiopentone, suxamethonium 1 mg kg$^{-1}$ was given i.v. The lungs were ventilated with halothane in nitrous oxide in oxygen. Five minutes later the same dose of suxamethonium was repeated, E.C.G. was monitored continuously. No serious bradycardia was observed following a second injection of suxamethonium in any group. The results suggest that thiopentone protects against suxamethonium-induced bradycardia during halothane anaesthesia.

Severe arrhythmia and asystole are well-known complications of repeated doses of suxamethonium (Martin, 1958; Bullough, 1959; Lupprian and Churchill-Davidson, 1960; Mathias and Evans-Prosser, 1968). In previous studies, we have examined the protective effect of atropine and gallamine when given before halothane (Viby-Mogensen et al., 1976; Wisborg, Christensen and Viby-Mogensen, 1977). Only atropine in doses causing considerable tachycardia protected against bradycardia and gallamine did not give sufficient protection even in doses causing severe tachycardia and a high frequency of unpleasant side-effects. These results seem inconsistent with those reports in which atropine and small doses of non-depolarizing neuromuscular blockers have been found to protect against severe arrhythmia following repeated doses of suxamethonium (Verner and Comty, 1959; Lupprian and Churchill-Davidson, 1960; Mathias, Evans-Prosser and Churchill-Davidson, 1970; Karhunen, Heinonen and Tammisto, 1972; Stoelting, 1977). However, our studies were conducted in patients who did not receive a barbiturate, whereas the patients in the other studies did, and did not receive halothane. Williams and others (1961) and Shoenstadt and Whitcher (1963) found that thiopentone protected against severe changes in cardiac rhythm following suxamethonium.

We have studied the effect of a second dose of suxamethonium after preoperative administration of atropine, gallamine or an i.v. combination in patients in whom anaesthesia was induced with thiopentone and maintained with halothane.

PATIENTS AND METHODS

Patients

Eighty healthy patients who underwent minor surgical procedures and gave consent to the study were allocated randomly to four groups.

Premedication was given i.m. 1 h before induction of anaesthesia and the drugs under study were given i.v. 3 min before injection of thiopentone (table I).

Anaesthesia (fig. 1)

Three minutes before induction atropine or gallamine or both was administered i.v. according to group. Anaesthesia was induced by slow injection of thiopentone 4–5 mg kg$^{-1}$ i.v. until the
eyelash reflex was abolished. Ventilation of the lungs was assisted or controlled throughout the study with halothane 1% in 50% nitrous oxide in oxygen using a non-rebreathing technique.

One minute after the injection of thiopentone was completed and exactly 5 min after, suxamethonium 1 mg kg⁻¹ was given i.v. The trachea was not intubated nor surgery performed during the observation period.

**Measurements**

E.c.g. lead II was monitored continuously throughout the procedure. Heart rate was determined from the e.c.g. (Wisborg, Christensen and Viby-Mogensen, 1977).

Blood samples were taken for measurement of serum potassium concentration, \( P_{\text{aco}_2} \), and \( P_{\text{ao}_2} \), before injection of atropine or gallamine, or both, and again 3 min after each injection of suxamethonium. Serum potassium was measured by the flame photometric method and blood-gases measured with a Radiometer ABL 1 acid–base machine. Arterial pressure was recorded every 5 min.

In order to exclude changes in cardiac rate and rhythm caused by gross alterations in \( P_{\text{aco}_2} \), the results include only those patients in whom \( P_{\text{aco}_2} \) was between 3.3 and 6.7 kPa (25 and 50 mm Hg) throughout the procedure.

Statistical analyses were performed using the \( \chi^2 \)-test, Fisher exact probability test, Kruskal-Wallis test and Wilcoxon matched-paired signed-ranks test. Significance was assigned at a level of 0.05.

### RESULTS AND DISCUSSION

**Cardiac rate and rhythm**

**Preinduction period.** There were no significant differences between the control values of the groups (fig. 2). After injection of atropine or gallamine, or both, the heart rate increased significantly in all groups \((P<0.01)\). One minute after injection the heart rate in group IV was significantly greater than in other groups.

The maximum changes in heart rate during this period are shown in figure 3. Increases in heart rate to more than 120 beat min⁻¹ were found in one patient in group II, in four patients in groups I and III, and in eight patients in group IV. However, these differences were not significant. Five patients in group I, and one patient in group IV had episodes of nodal rhythm after the injection of atropine or gallamine or both.

**Induction and first injection of suxamethonium.**

Only minor changes in heart rate were found after the first injection of suxamethonium. No serious arrhythmia was found. In group I, one patient had nodal rhythm continuing from the period before induction to 30 s after the injection of thiopentone. In group III, two patients developed nodal rhythm 27 and 43 s after the injection of suxamethonium which continued throughout the observation period. The remaining patients had regular sinus rhythm at all times.

**Second injection of suxamethonium.** After the second injection of suxamethonium, mean heart rate decreased in all groups (fig. 2). The lowest
rates occurred 30 s after injection in groups I and II, and 45 s after injection in groups III and IV. Compared with the values just before injection of the second dose of suxamethonium, the decrease in heart rate was significant only in group I ($P < 0.01$).

Thirty seconds after the second injection of suxamethonium, the heart rates in groups I and II were significantly less than the heart rates in groups III and IV.

The maximum decreases in heart rate after the second injection of suxamethonium are shown in figure 4, with the number of patients who had episodes of nodal rhythm. No patient had serious
bradycardia (less than 20 beat min⁻¹) or ventricular arrhythmia.

\[ P_{a_{CO_2}}, P_{a_{O_2}}, \text{and serum potassium} \]

Only minor variations occurred, and no significant differences were found between the groups.

**Arterial pressure**

The changes in arterial pressure were small, and no systolic arterial pressure of less than 12 kPa (90 mm Hg) was found.

None of the methods used provided absolute protection against a decrease in heart rate after the second injection of suxamethonium (fig. 4). However, the decrease in heart rate was significant only in group I (atropine 0.01 mg kg⁻¹ i.v.) and no patient developed severe bradycardia. Since all four methods investigated were able to protect against extreme bradycardia, we must consider if one method is superior. Both with and without premedication with atropine i.m., gallamine 0.3 mg kg⁻¹ i.v. 3 min before the injection of thiopentone provided greater protection. Atropine 0.01 mg kg⁻¹ i.v. alone (group I) did not give the same degree of protection (figs 2 and 4) and administration of both atropine and gallamine i.v. (group IV) caused unnecessary tachycardia which could be dangerous in certain patients (Viby-Mogensen et al., 1976).

In earlier similar investigations we found that atropine and gallamine, given during halothane anaesthesia in the same doses used in this investigation, did not provide sufficient protection against severe bradycardia following a second dose of suxamethonium (Viby-Mogensen et al., 1976; Wisborg, Christensen and Viby-Mogensen, 1977). Figures 5, 6, and 7 illustrate the changes in heart rate seen after a second dose of suxamethonium in patients from a previous study who received halothane and nitrous oxide only, compared with changes seen in patients from this investigation in whom thiopentone 4–5 mg kg⁻¹ preceded the administration of halothane. The mean heart rate, before the injection of atropine or gallamine, or both, was not significantly different in the four groups. After induction (fig. 5), the mean heart rate was significantly faster in patients who received thiopentone. Forty-five seconds after the second injection of suxamethonium, corresponding to the slowest heart rate in figure 5, the rate was still significantly faster in the patients who received thiopentone. The decrease in heart rate after a second dose of suxamethonium in patients receiving thiopentone was either not significant (gallamine group) or was significantly less (atropine group) than the decrease seen in patients who did not receive thiopentone. None of the patients who received thiopentone developed severe bradycardia (heart rate less than 20
Atropine, Gallamine and Suxamethonium

ATROPINE, GALLAMINE AND SUXAMETHONIUM

1141

Atropine 0.01 mg kg⁻¹ i.v.

Gallamine 0.3 mg kg⁻¹ i.v.

121-140

101-120

80

60

40

20

< 20

Inhalation induction

I.v. induction

121-140

101-120

80

60

40

20

< 20

Inhalation induction

I.v. induction

Fig. 5. Significance of thiopentone induction on bradycardia following a repeated dose of suxamethonium during halothane anaesthesia in patients given atropine 0.01 mg kg⁻¹ i.v. or gallamine 0.3 mg kg⁻¹ i.v. before operation. (No. of patients = 80; 20 in each group.) Mean values ± SEM are shown. SI and SII = suxamethonium 1 mg kg⁻¹ i.v. (first and second injection).

Fig. 6. Maximum decrease in heart rate after second injection of suxamethonium in two groups of patients (20 each) given atropine 0.01 mg kg⁻¹ i.v. and anaesthetized with halothane and nitrous oxide. One group of patients received an inhalation induction, the other received thiopentone 4-5 mg kg⁻¹ i.v. for induction. Each line represents one patient. --- = Nodal rhythm or nodal extrasystoles.

Fig. 7. Maximum decrease in heart rate after second injection of suxamethonium in two groups of patients (20 each) pretreated with gallamine 0.3 mg kg⁻¹ i.v. and anaesthetized with halothane and nitrous oxide. One group of patients received an inhalation induction, the other received thiopentone 4-5 mg kg⁻¹ i.v. for induction. Each line represents one patient. --- = Nodal rhythm or nodal extrasystoles; ---- = ventricular extrasystoles.

beat min⁻¹), whereas four and five patients in the two other groups (figs 6, 7) did so.

There are two possible explanations for the fact that atropine and gallamine in the doses investigated provided sufficient protection against severe bradycardia after a second dose of suxamethonium in patients induced with thiopentone but not in patients induced with halothane and nitrous oxide. The most obvious is that the difference is attributable to the vagolytic properties of thiopentone (Andersen and Eikard, 1978). However, patients in whom anaesthesia was induced with halothane and nitrous oxide were
exposed to halothane for a longer period (10–15 min) at the time of injection of the second dose of suxamethonium than patients induced with thiopentone (5–10 min). Therefore, a more pronounced influence of halothane on the heart cannot be excluded in that group.

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REFERENCES


EFFECTS CARDIACOS DE LA ATROPINA Y DE LA GALAMINA EN PACIENTES BAJO ADMINISTRACIÓN DE SUXAMETONIO

SUMARIO

Se distribuyó al azar a ochenta pacientes sanos en cuatro grupos. Antes de la operación, se administró 0,01 mg kg⁻¹ de atropina i.v. (grupo I), 0,3 mg kg⁻¹ de galamina i.v. (grupo II), 0,01 mg kg⁻¹ de atropina i.m. y 0,3 mg kg⁻¹ de galamina i.v. (grupo III), o 0,01 mg kg⁻¹ de atropina y 0,03 kg⁻¹ de galamina i.v. (grupo IV). Después de la inducción de la anestesia mediante tiopentona, se administró 1 mg kg⁻¹ de suxametonio i.v. Se ventilaron los pulmones con halotano en óxido nitroso en oxígeno. Se repitió la misma dosis de suxametonio cinco minutos después. Se vigiló continuamente el e.c.g. No se observó arritmia grave después de la segunda inyección de suxametonio en los grupos I y II. Los resultados sugieren que la tiopentona protege contra la bradicardia inducida por el suxametonio durante la anestesia por halotano.