COMPARATIVE STUDY OF ATROPINE AND GLYCOPPYRROLATE ON SUXAMETHONIUM-INDUCED CHANGES IN CARDIAC RATE AND RHYTHM

D. A. COZANITIS, J. W. DUNDEE AND M. M. KHAN

SUMMARY

The effectiveness of atropine and glycopyrrolate in the prophylaxis of suxamethonium-induced bradycardia was evaluated in a double-blind study of 56 patients. Three had clinically demonstrable bradycardia, all having received atropine. We conclude that glycopyrrolate offered adequate protection against cardiac effects of repeated doses of suxamethonium.

In 1958, Martin reported that suxamethonium-induced bradycardia could be reduced by the use of atropine as a premedicant. Bullough (1959) condemned the practice of giving repeated doses of suxamethonium unless a minimum of 0.65 mg of atropine had been administered. Lupprian and Churchill-Davidson (1960) confirmed that atropine could prevent bradycardia when given in a dose of 1 mg i.v. before the second dose of suxamethonium.

Glycopyrrolate, an antimuscarinic agent, has been evaluated extensively recently (Klingenmaier et al., 1972; Mirakhur, Dundee and Clarke, 1977; Cozanitis et al., 1980). There is, however, no evidence that it prevents changes in heart rate and rhythm associated with suxamethonium. Therefore we have compared the efficacy of atropine and glycopyrrolate on suxamethonium-induced cardiac effects.

PATIENTS AND METHODS

Fifty-six patients about to undergo minor surgery were studied. All were premedicated orally approximately 1 h before induction of anaesthesia with either diazepam 5–10 mg or meprobamate 800 mg. Two minutes before induction, they received either glycopyrrolate 0.005 mg kg⁻¹ or atropine 0.01 mg kg⁻¹ into a i.v. infusion of a physiological electrolyte solution. Allocation to the study drugs was randomized and double-blind.

The induction of anaesthesia, following a 2-min period of oxygenation, was with a sleep-dose of thiopentone, demonstrated by loss of the eyelash reflex. Suxamethonium 1 mg kg⁻¹ was given i.v. to facilitate tracheal intubation. Anaesthesia was maintained with 33% oxygen in nitrous oxide, with 25–50-mg increments of thiopentone, when necessary. A peripheral nerve stimulator (Wellcome) was applied to the bridge of the nose at intervals and on return of the contractions of the orbicularis oculi, a second and third dose of suxamethonium 0.5 mg kg⁻¹ were given. Monitor chest leads were used to record a single-channel electrocardiogram (e.c.g.) at intervals throughout the study. Atropine was always immediately available for use in case of severe and sustained decrease of heart rate. At the end of the study period, the planned surgical procedure was carried out.

The number of patients showing bradycardia, as defined by a heart rate less than 55 beat min⁻¹, was determined. Mean heart rate was measured by averaging 10 R-R intervals, 30 s after the administration of the antimuscarinic agent and similarly following thiopentone. If a wide fluctuation of heart rate occurred, the range was recorded and the mean heart rate was measured during the following 30 s. Heart rate was determined every 15 s after each increment of suxamethonium. Changes in cardiac rhythm were recorded.

The split-plot analysis of variance and the Mann–Whitney U test were used for statistical analysis when appropriate.

RESULTS

Table I shows some relevant details of the patients. The mean weight in the glycopyrrolate series was less...
Table I. Some details of the patients studied

<table>
<thead>
<tr>
<th></th>
<th>Atropine</th>
<th>Glycopyrrolate</th>
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</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>28</td>
<td>28</td>
</tr>
<tr>
<td>Mean age ± SEM (yr)</td>
<td>39 ± 2.4</td>
<td>40 ± 2.2</td>
</tr>
<tr>
<td>Mean weight ± SEM (kg)</td>
<td>65 ± 1.9</td>
<td>57 ± 2.2</td>
</tr>
<tr>
<td>Males</td>
<td>12</td>
<td>5</td>
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<tr>
<td>Mean time ± SEM (min)</td>
<td>3.9 ± 0.15</td>
<td>3.9 ± 0.16</td>
</tr>
<tr>
<td>Study drug–1st sux. dose</td>
<td>3.6 ± 0.23</td>
<td>3.9 ± 0.23</td>
</tr>
<tr>
<td>1st sux. dose–2nd dose</td>
<td>3.6 ± 0.8</td>
<td>3.3 ± 0.29</td>
</tr>
<tr>
<td>2nd sux. dose–3rd dose</td>
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than that of those having received atropine because of a greater proportion of females in the former group. There were no major differences in the times between administration of the study drugs and the first administration of suxamethonium and between the subsequent doses of suxamethonium.

Both drugs produced an increase in heart rate of about 10 beat min⁻¹ after administration, but this change was neither clinically nor statistically significant. Indeed, there were no statistically significant differences in the mean heart rates between the two series at any time (fig. 1).

No patient developed bradycardia following the first dose of suxamethonium but the second dose did result in bradycardia in three patients, all in the atropine series. Bradycardia was seen in two of these patients again after the third suxamethonium dose. The bradycardia always developed within 45 s of injection of the suxamethonium and was transient, the heart rate reverting to pre-suxamethonium values within 75 s.

In those patients with clinically significant bradycardia, one patient had sinus arrest lasting 3.2 s after the second increment of suxamethonium and another episode of sinus arrest of 2.2 s following the third dose of the relaxant. One patient developed nodal bradycardia while another showed sinus bradycardia. A further five patients had e.c.g. abnormalities; four of these were in the atropine series—two presented with nodal rhythm, one had atrial ectopic beats and one, ventricular extrasystoles. The fifth patient, in the glycopyrrolate series, had nodal rhythm after administration of this antimuscarinic agent and during induction with thiopentone.

![Fig. 1. Changes of mean heart rates of the patient series at the different intervals of the study period.](https://academic.oup.com/bja/article-abstract/52/3/291/243630)
DISCUSSION

The results show that, although bradycardia occurred in three of the patients receiving atropine following the subsequent doses of suxamethonium as compared with none in the glycopyrrolate series, the mean heart rate changes in the two groups were not statistically significant. It is important to note that clinically significant decreases in heart rate occurred in three patients even though they had been pretreated with i.v. atropine immediately before the induction of anaesthesia.

An interesting observation was made on the cardiac rhythm of two patients, one from each series, who developed nodal rhythm after the i.v. injection of the antimuscarinic study drug. It appears that, initially, antimuscarinics cannot drive the sinus node but influence the A-V junctional node, but later the sinus node begins to take over. Neither of these patients showed any evidence of sinus node dysfunction in the resting ECG.

One patient developed sinus arrest lasting 3.2 s after the second dose of suxamethonium, and this occurred again for 2.2 s, following the third increment of suxamethonium. Nodal bradycardia followed these episodes. It appears that this is a result of the parasympathetic effect of the relaxant on the sinus node.

It is apparent from this study that glycopyrrolate offers protection against the cardiac effects resulting from intermittent administration of suxamethonium similar to or greater than that of atropine. One could argue that a controlled study using a series of patients not having received any antimuscarinic medication is necessary before the absolute efficacy of these two drugs can be evaluated. However, this possibility was discounted as being unethical.

ACKNOWLEDGEMENT

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REFERENCES


ETUDE COMPARATIVE DE L'ATROPINE ET DU GLYCOPPYRROLATE EN CE QUI CONCERNE LES MODIFICATIONS DUES AU SUXAMETHONIUM DU RYTHME ET FONCTION CARDIAQUES

RESUME

On a procedé à l'évaluation au moyen d'une étude à double inconnue sur 56 patients de l'efficacité de l'atropine et du glycopyrrolate dans la prophylaxie de la bradycardie provoquée par le suxamethonium. Trois patients souffraient de bradycardie cliniquement évidente et tous avaient reçu de l'atropine. Nous en avons conclu que le glycopyrrolate offre une protection adéquate contre les effets cardiaques de doses réitérées de suxamethonium.

VERGLEICHENDE STUDIE VON ATROPIN UND GLYCOPPYROLAT BEI DURCH SUXAMETHONIUM BEWIRKTE VERÄNDERUNGEN VON HERZTÄTIGKEIT UND RHYTHMUS

ZUSAMMENFASSUNG


ESTUDIO COMPARATIVO DE LA ATROPINA Y DEL GLICOPIRROLATO SOBRE LOS CAMBIOS INDUCIDOS POR SUXAMETONIO EN EL RITMO CARDIÁCO Y FUNCION SISTOLICA

SUMARIO

Se procedió a la evaluación de la eficacia de la atropina y del glicopirrolato en la profilaxis de la bradicardia inducida por suxametonio en el curso de un estudio doble-ciego de 56 pacientes. Tres de ellos padecieron de bradicardia clínicamente demostrable, habiéndose administrado atropina a todos. Concluimos que el glicopirrolato ofrecía una protección adecuada contra los efectos cardíacos de repetidas dosis de suxametonio.