EFFECT OF ANAESTHESIA ON THE QT INTERVAL

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The QT interval, which is measured from the start of the Q wave (or the R wave when no Q wave is present) to the completion of the T wave, reflects the duration of electrical ventricular systole. The duration of systole varies with heart rate and therefore the measured QT interval is often corrected for heart rate using the following formula, in which QTc represents the rate corrected value:

\[ QTc = \frac{QT}{\sqrt{RR \text{ interval}}} \]

The QTc interval is normally less than 440 ms \[1\]. Increased serum concentrations of noradrenaline and a change in the balance between sympathetic and parasympathetic tone may be associated with prolonged QT interval \[2, 3\]; this may be controlled with either \(\beta\)-block \[4\] or stellate ganglion block \[5\]. Hypomagnesaemia and, more commonly, hypokalaemia cause clinically significant prolongation which may be produced by effects on the repolarizing potassium current. Sleep (which is associated with a reduction in sympathetic tone) prolongs QTc \[6\].

Induction of anaesthesia with thiopentone prolongs significantly the QT interval \[7\], whereas Althesin had no effect \[8\]. The most marked changes follow tracheal intubation facilitated with suxamethonium, but these changes may be reduced by pretreatment with tubocurarine \[7\] or by \(\beta\)-block \[9\], suggesting mediation by the sympathetic nervous system. It has been reported also that the QT interval is significantly prolonged by enflurane \[8, 10\], but not by halothane anaesthesia \[8\]. The mechanism underlying these differences has not been explained. It has been reported that these volatile agents and also isoflurane prolonged the QT and QTc intervals in dogs by a direct effect independent of autonomic activity \[11\].

The effects of the newer anaesthetic agents on QT intervals have not been studied in man. Propofol is used extensively both for induction and maintenance of anaesthesia for day case and other surgery. We have therefore compared the effects of propofol and thiopentone on the QT interval during induction and during subsequent maintenance of anaesthesia with enflurane or isoflurane.

PATIENTS AND METHODS

The study was approved by the hospital Ethics Committee. Informed consent was obtained from 121 female patients (ASA I or II, not receiving intercurrent medication) undergoing elective gynaecological and general surgery (breast biopsy) under mask inhalation anaesthesia. They were allocated randomly to four groups to receive the following anaesthetic drug combinations:

- **Group 1 (n = 31)**: Thiopentone 5 mg kg\(^{-1}\) for induction; enflurane and nitrous oxide in oxygen for maintenance.
- **Group 2 (n = 30)**: Thiopentone 5 mg kg\(^{-1}\) for induction; isoflurane and nitrous oxide in oxygen for maintenance.
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Group 3 (n = 30). Propofol 1.5 mg kg⁻¹ for induction; enflurane and nitrous oxide in oxygen for maintenance.

Group 4 (n = 30). Propofol 1.5 mg kg⁻¹ for induction; isoflurane and nitrous oxide in oxygen for maintenance.

Patients were premedicated with temazepam 20 mg orally 1–2 h before anaesthesia. In the anaesthetic room the patients were connected to an ECG monitor and standard lead II control recordings were obtained. Anaesthesia was induced and a further ECG recording obtained at the time of loss of the eyelash reflex. The volatile agent mixtures were introduced subsequently and a third ECG record was made after 10 min of deep inhalation anaesthesia. At this stage the study was terminated.

Analysis of ECG records

All the records were coded and analysed “single blind” by one author (I. McC.). Measurement of the QT interval may sometimes be difficult because of doubt on the end point of the T wave. Therefore, the point at which the line of maximum downslope of the T wave crossed the isoelectric baseline was chosen according to recent guidelines [12]. The QT interval was corrected for rate as described above. Three consecutive cycles were analysed and averaged [12]. The data were collated and analysed using one- and two-way analyses of variance and Student’s t test. Statistical significance was assumed at the conventional 5% level.

RESULTS

There were no significant differences in QTc between the four groups at the control assessment (F (3, 117) = 0.98) (P = 0.41) (table I). To evaluate the changes between control and postinduction values, the difference between these measurements was calculated and treated as a new variable. Thus for this purpose the two groups receiving thiopentone were combined, as were those receiving propofol. Both thiopentone and propofol induced a significant prolongation in mean QTc interval; the increase was significantly greater in those patients given thiopentone than in those given propofol (table II) [13].

The QTc interval after maintenance of anaesthesia with the volatile agents was considered also. The data were analysed using the four original groups, and the effects of the induction and maintenance agents on the QTc interval were examined separately. No significant difference was found for the changes between induction and maintenance, demonstrating that only the induction drug had a significant effect on QTc interval (F (1, 117) = 3.98) (P = 0.046).

The changes in heart rate did not exceed 5% of the control values in any of the four groups during the 10-min period of measurement.

DISCUSSION

A prolonged QT interval is a clinically important finding. Indeed, an abnormal QT interval may be the single most commonly missed marker of preventable cardiac death [12]. A prolonged QT interval occurring during acute myocardial infarction may be associated with ventricular arrhythmia [14] and may predict sudden death [15]. The combination of hypokalaemia following therapy with diuretics and antiarrhythmic drugs which prolong the QT interval (such as quinidine, disopyramide, sotalol and amiodarone) is particularly dangerous and may lead to an atypical ventricular tachycardia termed Torsade de Pointes. This is difficult to distinguish from ventricular fibrillation, but requires different therapy.

A prolonged QT interval may be discovered when patients present for preoperative ECG examination. It should be remembered that a prolonged QT may be congenital [16, 17] and may result in ventricular arrhythmia [18] and may lead to sudden death under anaesthesia [19].

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<tr>
<th>Table I. Mean (SD) QT intervals (ms), corrected for heart rate, for the four study groups at each assessment time</th>
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<tbody>
<tr>
<td>Group 1 Group 2 Group 3 Group 4</td>
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<tr>
<td>Control: 433.10 (27.35) 435.00 (28.86) 426.27 (29.67) 424.77 (25.62)</td>
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<tr>
<td>Induction: 468.81 (32.64) 471.20 (31.92) 443.57 (31.67) 449.93 (24.77)</td>
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<tr>
<td>Maintenance: 462.81 (31.85) 463.03 (40.71) 443.10 (32.46) 441.33 (25.82)</td>
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<tr>
<th>Table II. Mean increases in QTc (95% confidence limits) (ms) after induction with thiopentone or propofol. n = Number of patients. Test statistics: t (119) = 2.65; P = 0.009</th>
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<tbody>
<tr>
<td>Induction agent</td>
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<tr>
<td>Thiopentone (n = 61)</td>
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<td>Propofol (n = 60)</td>
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prolonged QT syndrome has been the subject of recent reviews and reports of interest to the anaesthetist [12, 20]. In order to avoid an adverse outcome it would be useful to know which, if any, anaesthetic agents are contraindicated in this circumstance [19]. Anaesthetic agents with negligible effects on the QT interval should be of clinical value when an anaesthetic is required for a patient with a prolonged QT interval—although it is dangerous to extrapolate effects in normal individuals to the effects on patients with clinically prolonged QT interval. Galloway has suggested that thiopentone should be the agent of choice for patients with prolonged QT interval [20], but the results presented here suggest that propofol has less effect on the QT interval and may therefore be a more appropriate choice. Tracheal intubation is associated usually with rapid changes in heart rate and these invalidate the correction involved in calculating QTc interval [21]. The patients in the present study did not develop rapid changes in heart rate compared with previous studies involving patients who underwent intubation and therefore these results are particularly relevant.

The choice of induction appears to be more important than the choice of maintenance agent, especially during the period of tracheal intubation.

It is not known how long the effects of the induction agents may mask any independent effects of enfurane or isofurane. However, no volatile agent is likely to be completely safe [11]. On theoretical grounds, isofurane may be the inhalation agent of choice as it has previously been used safely in the presence of a prolonged QT interval [22].

In conclusion, it has been shown that propofol prolongs the QT interval less than thiopentone and it is suggested, therefore, that this drug is more appropriate than thiopentone for a patient with either congenital or acquired prolonged QT interval.

REFERENCES