Sevoflurane, but not Propofol, Significantly Prolongs the Q-T Interval

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Prolongation of the Q-T interval may be associated with polymorphic ventricular tachycardia known as torsade de pointes, syncope and sudden death. Existing data show that isoflurane prolongs the Q-T interval, whereas halothane shortens it. The aim of this study was to determine whether sevoflurane or propofol affects the Q-T interval. Thirty female patients undergoing gynecologic surgery were randomly assigned to two groups, one receiving inhaled induction with sevoflurane and the other receiving total IV anesthesia with propofol. Before and 20 min after the induction, a six-lead electrocardiogram was recorded, and blood pressure was measured. The Q-T interval and heart rate adjusted Q-T interval (Q-Tc interval) were significantly prolonged during the administration of anesthesia with sevoflurane, while the Q-T interval was significantly shortened, and the Q-Tc interval was statistically unaffected during propofol anesthesia administration. We conclude that, in otherwise healthy female patients, sevoflurane prolongs the Q-Tc. **Implications:** In this study, we evaluated the effect of sevoflurane induction and anesthesia versus propofol induction and anesthesia on the Q-T interval. Sevoflurane significantly prolonged the Q-T interval and the heart rate adjusted Q-T interval, whereas propofol shortened the Q-T interval but not the heart rate adjusted Q-T interval.

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Prolongation of the Q-T interval is an alteration of the electrocardiogram (ECG) that may result in a potentially dangerous polymorphic ventricular tachycardia known as torsade de pointes. Additionally, prolongation of the Q-T interval is strongly associated with sudden infant death syndrome (1). Q-T interval prolongation may be congenital (congenital long Q-T syndrome [CLQ-TS]), representing mutations in four genes encoding cardiac potassium and sodium channels (2). The genotype of the long Q-T syndrome influences the clinical course of the disease (3). Acquired forms of the long Q-T syndrome follow the administration of drugs, such as droperidol (4), class Ia and III antiarrhythmics, antidepressants, and other medications (5), or it may result from metabolic disorders (2). Female patients have a longer Q-Tc interval and a higher incidence of torsade de pointes tachycardia than male patients (6) and more frequently develop torsade de pointes after the administration of drugs that modify potassium or sodium currents (conductance) to lengthen cardiac repolarization (7). In patients presenting with a prolonged heart rate adjusted Q-T (Q-Tc) interval, the choice of anesthetic is of importance. Michaloudis et al. (8) investigated the effect of isoflurane and halothane on the Q-T interval in nonpremedicated children, premedicated children (9), and in premedicated adults (10). Isoflurane significantly prolonged the Q-Tc interval, in contrast to halothane, which shortened the Q-Tc interval. No controlled study of the influence of sevoflurane on the Q-T interval has yet been published. In 1998, Abe et al. (11) reported a ventricular tachycardia torsade de pointes during sevoflurane/nitrous oxide anesthesia administration in a patient, and Gallagher et al. (12) reported on a patient with CLQ-TS, which was further prolonged during sevoflurane inhalation. Propofol has no significant effect on the Q-Tc interval in healthy adults (13) and tends to shorten an already prolonged Q-Tc interval (14). The aim of this study was to evaluate the effect of sevoflurane on the Q-T interval in healthy, female patients, as drug-induced torsades de

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pointes and symptomatic long Q-T syndrome have a female predominance (15).

Methods

This study was approved by the human investigation committee of the University of Innsbruck (Innsbruck, Austria) in September, 1998. After obtaining written, informed consent, 30 women classified as ASA physical status I or II were enrolled. Patients had been scheduled for elective gynecological surgery with an expected duration of approximately 60 min. Women presenting with cardiovascular impairment or chronic obstructive lung disease, women receiving medication, and women with an abnormal prolongation of the Q-Tc interval (≥440 ms) were excluded. All patients were premedicated orally with 0.1 mg/kg diazepam 30 to 60 min before the first measurement. Diazepam is not known to alter the Q-T interval. The patients were then randomly allocated to one of two groups, one receiving sevoflurane anesthesia and the other receiving propofol anesthesia. In all patients, a six lead (I, II, III, aVL, aVR, and aVF) ECG (Cardiosmart; Hellige GmbH, Freiburg, Germany) was recorded before administering oxygen/air at a fraction of inspired oxygen (F_{IO_2}) of 0.3 via a face mask. Identical ventilators (Julian; Dräger Medizintechnik, Lübek, Germany) and vaporizers (Dräger Medizintechnik) were used in all patients. Fresh gas flow was 8 L/min in both groups. In all patients, ventilation was controlled via a face mask after the induction with end-tidal concentration of carbon dioxide monitored and maintained at 40 mm Hg throughout the study. In the sevoflurane group, anesthesia was induced via a face mask by initially administering 1.0% sevoflurane, then by increasing the inspiratory concentration after every fifth breath by 0.5% until a maximum of 6% sevoflurane vapor was achieved. Once anesthesia had been induced, an end-tidal concentration of 2.5% sevoflurane vapor was maintained to provide an adequate depth of anesthesia. In order to establish steady state conditions, 20 min was allowed until the second six-lead ECG was recorded. In the propofol group, anesthesia was induced IV by using 2.5 mg/kg propofol at a constant rate of 20 mL/min while the patient was breathing oxygen/air at F_{IO_2} of 0.3. Anesthesia was maintained using a continuous infusion of propofol at a rate of 6 $mg \cdot kg^{-1} \cdot h^{-1}$. Twenty minutes after the induction, the second six-lead ECG was recorded. In all patients, a 1-mL blood sample was subsequently obtained via a venous catheter to measure the serum concentrations of sodium, potassium, magnesium, and calcium. After the measurements were completed, anesthesia was continued according to the individual needs of patient and type of surgical intervention by using opioids, muscle relaxants, tracheal intubation, or laryngeal mask airway as required.

The investigators reading the ECG were blinded to the type of induction and anesthesia used. The following variables were recorded or calculated: heart rate, P-R interval, QRS interval, Q-T interval, Q-Tc interval according to Bazett's formula (Q-Tc = Q-T/$\sqrt{}$R-Rsec), (16,17), systolic blood pressure, and diastolic blood pressure. Blood pressure was measured in a noninvasive fashion by using a Datex AS 3 monitor (Datex, Helsinki, Finland) that automatically calculates mean arterial pressure. Occurrence and type of arrhythmia was noted by observation of the monitor.

All values were expressed as mean ± SEM. A two-way analysis of variance for repeated measures was used for determination of intergroup and intragroup differences. A two-tailed test was used. P values smaller than 0.05 were considered significant. Significant *post hoc* differences were analyzed by using the Newman-Keuls test.

Results

There were no demographic differences between the two groups (Table 1). Cardiovascular and Q-T interval recordings and calculations are shown in Table 2. No intergroup or intragroup differences in P-R interval (150 ± 3 ms) and in QRS interval (79 ± 3 ms) were observed. P wave height was 1.3 ± 0.6 mm, and mean axis of QRS was 51 ± 4.7 degrees. Sinus rhythm was present in all patients. The Q-Tc interval did not exceed 440 ms in any of the patients. One patient in the propofol group developed a short run of three monomorphic ventricular ectopic beats after the induction of anesthesia, whereas in the sevoflurane group, no form of arrhythmia occurred. Sevoflurane and propofol induced significant decreases ($P < 0.01$) in systolic, mean, and diastolic blood pressure. Sevoflurane but not propofol significantly decreased heart rate. The plasma concentrations of sodium, potassium, calcium, and magnesium were within normal ranges in all patients and did not differ between the two groups.

Discussion

The main finding of this study was that, in healthy female patients, the induction and anesthesia with sevoflurane significantly prolongs the Q-T and the Q-Tc interval, whereas the induction and total IV anesthesia with propofol significantly shortens the Q-T but not the Q-Tc interval. Heart rate was reduced by sevoflurane ($P < 0.05$ in intragroup comparison), but not by propofol. No other ECG variables were altered by either sevoflurane or propofol. Both drugs induced significant decreases ($P < 0.01$) in blood pressure. In the propofol group, the largest recommended doses were applied, but the resulting cardiovascular depression was less than that in the sevoflurane

Table 1. Demographic Data

	Sevoflurane group	Propofol group
Patients (*n*)	15	15
Age (yr)	36.3 ± 2	37.6 ± 3
Weight (kg)	68.8 ± 5	63.3 ± 2

Values are mean ± SEM.

Table 2. Cardiovascular and Q-T Interval Recordings and Calculations

Anesthetic	Before induction	20 min after induction
QT interval (ms)		
Propofol	377 ± 5	360 ± 6‡
Sevoflurane	370 ± 8	411 ± 7*‡
QTc (ms)[a]		
Propofol	413 ± 6	403 ± 8
Sevoflurane	409 ± 4	435 ± 5*‡
Heart rate (bpm)		
Propofol	72 ± 2	75 ± 3
Sevoflurane	75 ± 4	68 ± 2†
Systolic blood pressure (mm Hg)		
Propofol	123 ± 3	105 ± 4‡
Sevoflurane	130 ± 4	99 ± 2‡
Mean arterial pressure (mm Hg)		
Propofol	90 ± 2	76 ± 3‡
Sevoflurane	94 ± 3	70 ± 2‡
Diastolic blood pressure (mm Hg)		
Propofol	75 ± 2	66 ± 2‡
Sevoflurane	78 ± 2	59 ± 2‡

Values are mean ± SEM.
* $P < 0.01$ in intergroup comparison.
† $P < 0.05$, ‡ $P < 0.01$ in intragroup comparison.
[a] Q-Tc reflects the heart rate adjusted Q-T interval by using Bazett's formula.

group, although the intergroup difference was not significant. Our findings differ considerably from those made by Thwaites et al. (18), who found that the depression of the mean arterial pressure caused by propofol is more pronounced than with sevoflurane. This may be caused by the different induction techniques used, because in our experiment, the inspiratory concentrations of sevoflurane were raised incrementally at the induction of anesthesia. Propofol had no significant effect on Q-Tc interval in our study, which is compatible with the findings of Michaloudis et al. (13). Propofol shortened the Q-T interval in our study, which is consistent with the findings of Saarnivaara et al. (14) who found that, among other drugs, propofol shortens an already prolonged Q-T interval.

We conclude that, in otherwise healthy female patients, sevoflurane prolongs Q-Tc. The amount of sevoflurane-associated Q-T prolongation may possibly be of clinical significance in some patients presenting with CLQ-TS, hypokalemia, or in the presence of other agents or factors that lengthen Q-T (acquired forms of the long Q-T syndrome).

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