

Inhalation of Sevoflurane and Desflurane Can Not Affect QT Interval, Corrected QT, Tp-Te/QT or Tp-Te/JT in Children

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To the Editor: Sevoflurane and desflurane are the most common general anesthetics used in children. Previous study has shown that these agents can affect the electrocardiogram (ECG) markers,^[1] leading to fatal ventricular arrhythmia. The followings were identified as useful indices for predicting and estimating the occurrence of a fatal arrhythmia: the interval between the peak and the end of T wave (Tp-Te),^[2] the ratio of the Tp-Te interval to the QT interval ($[Tp-Te/QT]^{[3]}$), and the JT interval (JT), which is measured from the end of the QRS complex to Te.^[4] The QT interval may be affected by sex and age.^[5] However, little is known about the co-effect of the inhaled agent and sex on the corrected QT (QTc) and Tp-Te/QT and Tp-Te/JT ratios.

This study explored the co-effect of inhaled anesthetics and sex on the prolongation of the QTc and the Tp-Te/QT and Tp-Te/JT ratios in children during anesthesia. Ethical approval for this study (No. H1412-021-631) was obtained from the Institutional Review Board of Seoul National University Hospital, Seoul, Korea, and registered at <http://cris.nih.go.kr> (No. KCT0001430). Pediatric patients (2–12 years) scheduled for minor surgery (<2 h) under general anesthesia were enrolled in this study. The exclusion criteria were as follows: a prolonged QT interval sufficient to induce fatal arrhythmia, electrolyte imbalances, hypothyroidism, the patient was taking medication that affects QT intervals, and a preoperative QTc >450 ms. Patients were randomized to either the sevoflurane or desflurane group, with an equal number of boys and girls, using a random number table. Data from lead II of a 3-min reading of 3-lead ECG were obtained, while the patient was in the reception area for the baseline reading and again 1 h after the induction of anesthesia. The ECG data were analyzed using LabChart® (version 7.0; ADInstruments, Colorado Springs, CO, USA) after the removal of artifacts. The QT interval was calculated as the time from the start of the QRS complex to Te and the QTc was calculated using Bazett's formula. The Tp-Te/QT and Tp-Te/JT ratios were also calculated. All data are expressed as the average of four successive heartbeats.

The primary endpoint was the effect of the interaction between sex and inhaled anesthetics on changes in the QT interval, QTc, and Tp-Te/QT and Tp-Te/JT ratios between baseline and after anesthesia. The secondary endpoint was the difference between the QT interval, QTc, and Tp-Te/QT and Tp-Te/JT ratios of boys to girls and inhaled anesthetics during each period.

After testing for normality using the Shapiro-Wilk test, the normally distributed data were presented as mean \pm standard deviation. The primary outcome was analyzed using a two-way analysis of variance and the secondary outcomes were analyzed using the Student's *t*-test. $P < 0.05$ was considered statistically significant.

In total, 125 (sevoflurane, $n = 63$; desflurane, $n = 62$; M:F ratio = 61:64) out of 128 children completed the study. Sex, the inhaled anesthetic agent, and interaction between those factors did not influence the QT interval, QTc, or Tp-Te/QT and Tp-Te/JT ratios.

QT interval, QTc, and Tp-Te/QT and Tp-Te/JT ratios at baseline were similar between the boys and girls. During anesthesia, only the QT interval differed between the sexes [Table 1]. The changes in the QT interval, QTc, and Tp-Te/QT and Tp-Te/JT ratios were not significantly different between the boys and girls. During anesthesia, QT intervals were similarly prolonged in all the children. The anesthetic agent also had no effect on the QT interval, QTc, or Tp-Te/QT and Tp-Te/JT ratios during anesthesia.

The inhaled anesthetics and sex had no co-effect on the QT interval, QTc, or Tp-Te/QT and Tp-Te/JT ratios in children. Clinically, this favorable result suggests that sevoflurane and desflurane are safe in all children.

Due to sex hormones and gonadotropins present during the period from puberty to menopause, the QTc intervals are longer in women than those in men. Dickson reported that sex does not appear to be a significant factor for determining the QT interval in prepubertal and adolescent groups. In this study, QT interval, QTc, and Tp-Te/QT and Tp-Te/JT ratios at baseline were similar between boys and girls. Although the QT intervals in boys were longer than those in girls during anesthesia, QTc values were within the normal range and showed no differences based on sex.

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Table 1: QT interval, corrected QT interval, and Tp-Te/QT and Tp-Te/JT in boys and girls during baseline and anesthesia periods

Items	Boys (n = 61)	Girls (n = 64)	P
QT interval (ms)			
Baseline	321.9 ± 39.1	309.1 ± 42.1	0.829
Anesthesia	323.8 ± 38.4	317.8 ± 50.5	0.041*
Difference	6.3 ± 32.9	12.1 ± 32.0	0.672
QTc (ms)			
Baseline	409.7 ± 20.2	400.0 ± 22.7	0.389
Anesthesia	444.1 ± 30.0	433.6 ± 30.0	0.652
Difference	36.8 ± 27.4	35.1 ± 27.3	0.566
Tp-Te/QT			
Baseline	0.21 ± 0.04	0.21 ± 0.04	0.903
Anesthesia	0.18 ± 0.06	0.18 ± 0.04	0.191
Difference	-0.03 ± 0.06	-0.03 ± 0.05	0.494
Tp-Te/JT			
Baseline	0.28 ± 0.06	0.28 ± 0.05	0.610
Anesthesia	0.24 ± 0.08	0.24 ± 0.06	0.208
Difference	-0.03 ± 0.06	-0.03 ± 0.05	0.494

Values were shown as mean ± SD. *P<0.05 compared to baseline values. SD: Standard deviation.

Many studies have investigated whether different inhaled agents have different effects on ECG-derived parameters such as the QTc, Tp-Te ratio, JT, or QT dispersion. In the study, the QT interval, QTc, and Tp-Te/QT and Tp-Te/JT ratios were similar between sevoflurane and desflurane. Differences between our and previous results might be due to a variation in study designs, data collection time, or QT interval correction formula.

Bazett's formula is derived for the adult population and is not suitable for children with high heart rates. Nevertheless, Bazett's formula still has the power to calculate the QTc in children. Similar to previous studies, the QTc interval was calculated using Bazett's formula in the present study.

Recently, Staikou *et al.*^[1] have reported the impact of anesthesia on torsadogenicity, as determined by ECG markers. The authors concluded that the lack of any effect on transmural dispersion of repolarization of heart possibly indicates that sevoflurane has no significant intrinsic torsadogenicity. On the contrary, desflurane was associated with a persistent QTc prolongation in children and

a weak correlation between the increase of QT dispersion and occurrence of an arrhythmia was found. Therefore, desflurane might be more torsadogenic than sevoflurane.

This study had several limitations. First, since there is no standard formula to calculate QTc in children, Bazett's formula was used. The second weakness was that we did not explore the interactions among sex, age, and type of inhaled anesthetic agent. Finally, we routinely used atropine during the induction of anesthesia; this could have affected the calculation of ECG-derived parameters.

In conclusion, sevoflurane or desflurane and sex cannot co-affect the QT interval, QTc, and Tp-Te/QT and Tp-Te/JT ratios in children during anesthesia.

Declaration of patient consent

Written informed consent was obtained from the parents and children >7 years of age. The patients' guardians have given their consent for reporting their images and other clinical information in the journal. The patients' guardians understand that their names and initials will not be published and due efforts will be made to conceal their identity.

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Conflicts of interest

There are no conflicts of interest.

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