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Comparison of the Effect of Sevoflurane and Desflurane on Postoperative Arrhythmia and QT Dispersion

Research Article

Muhammet Gozdemir[2], Ekrem Yeter[1], Murat Akcay[1], Elvin Kurdoglu[2], Tülin Gumus[2], Telat Keleş[1], Emine Bilen[1], Orhan Kanbak[2]

[1] *Atatürk Education and Research Hospital, Department of Cardiology, 06800, Ankara, Turkey*

[2] *Atatürk Education and Research Hospital, Department of Anesthesiology, 06800, Ankara, Turkey*

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Abstract: The aim of this study was to investigate the effect of sevoflurane and desflurane on cardiac arrhythmias in adult patients who will be anesthetized. A total of 40 patients who were in the ASA I-II group and who were to undergo elective surgery were included in the study. No pre-medication was administered to the patients. They were monitored with the Holter equipment at preoperative 24 hours, and also at postoperative 24 hours on condition that Holter monitoring will begin before induction. Following routine monitoring, the patients were randomly divided into two equal groups; group one was given sevoflurane and group two was given desflurane. In this study, desflurane and sevoflurane resulted in both a significant prolongation of QT and QTc and a significant increase in QT and QTc dispersion when compared with the basal values. In the sevoflurane group, there was no significant increase in postoperative ventricular arrhythmia, compared to that during the preoperative period. However, this increase was significant in the desflurane group ($p = 0.009$). Sevoflurane and desflurane result in an increase in QT dispersion. Postoperative rhythmic control should carefully be monitored, especially in the desflurane group.

Keywords: *Desflurane • Sevoflurane • QT • Holter • Arrhythmia*

1. Introduction

Perioperative ventricular dysarrhythmias are thought to be electrical indicators of structural heart diseases or of temporal physiological irregularities of the heart. Although the mechanism of dysarrhythmias in patients with structural heart diseases is clearly defined, little confirmed knowledge has been documented about dysarrhythmias caused by temporal physiological irregularities while the patient is under anesthesia [1,2].

The QT interval is affected by autonomic conditions, catecholamines, and by diurnal rhythm; it also is different in males and females. A prolonged QT interval may be congenital or acquired, and may lead to malignant ventricular arrhythmia, serious polymorphic ventricular tachycardia, Torsade de Pointes, and syncope. Many acquired forms of prolonged QT syndrome may arise following use of drugs, among them droperidol, class Ia and class III anti-arrhythmics, and antidepressants [3,4]. Anesthesia and surgery introduce potential stimulants that exacerbate tachydysrhythmias in these patients [5].

Most anesthetic agents that are used in clinical anesthetic practice affect the QT interval. Studies have been carried out in cases where life-threatening arrhythmias may have caused sudden death during general anesthesia in patients with a normally prolonged QT interval [6]. Hence, it is recommended that further studies should be performed to investigate this problem. Unfortunately, very few studies have been carried out to explore the effect of volatile anesthetic agents on the QT interval. Among the few are studies conducted to

* *E-mail: ekremyeter@hotmail.com*

investigate the effect of the volatile anesthetic agents halothane, sevoflurane, isoflurane, and enflurane on the QT interval [7,8]. In this study, we investigate the effect of sevoflurane and desflurane on cardiac arrhythmias in adult patients who will be anesthetized.

2. Material and Methods

The final study population was 40 patients, aged 18 to 60 years, who were in the ASA I-II group and were to undergo elective (without cardiovascular and emergency) surgery. All patients gave written consent; approval by the ethics committee of our hospital (Ankara Ataturk Training and Research Hospital) was obtained. The following patients had previously been excluded: those with a preoperative QT interval > 400 milliseconds, those whose preoperative Holter data demonstrated serious arrhythmias (such as ventricular and supraventricular tachycardia), those using drugs that could affect the QT interval (anti-arrhythmic drugs, beta blockers, positive inotropic agents, tricyclic antidepressants, phenothiazines). Also excluded were patients with rhythms other than sinus rhythm; patients with pre-excitation and bundle branch block, cardiac valve disease, pericardial effusion, presence of cardiac ischemia, electrolyte anomaly; patients who had diabetes or a history of endocrine disease; pregnant women; and patients with morbid obesity.

The patients were not given pre-medication and were monitored with the Imagata CF Holter equipment 24 hours preoperative, and also 24 hours postoperative on condition that Holter monitoring will begin before induction. The Holter data were registered digitally using the Cardioscan 11.0 computer program.

Before being taken into the operating room, the 12 derivation ECGs of all patients were obtained using the Schiller AT-2 plus standard ECG equipment before induction, and after intubation, at the 1st, 3rd and 5th minutes after 1 minimum alveolar concentration (MAC) stable end-tidal anesthetic concentration was attained, after extubation, and at 50 $mm.sec^{-1}$ postoperative 24 hours after Holter.

Following routine monitoring, the patients were randomly divided into two equal groups; one group received anesthetic induction with thiopental 5–7 $mg.kg^{-1}$ and the other, vecuronium 0.08–0.10 $mg.kg^{-1}$. The patients were intubated 3 minutes after vecuronium application. Maintenance anesthesia was provided by addition of 2% (1 MAC) sevoflurane to the 1:1 mixture of N_2O-O_2 in group one, and 6% (1 MAC) desflurane in group two. Both operator and patient were aware of the assigned maintenance anesthesia before the patient was taken into the operating room. Controlled ventilation was provided in both groups by adjusting a fresh gas flow at 6 $L.min^{-1}$ in all patients throughout the surgery to maintain the end-tidal CO_2 pressure at 30-35 mmHg.

The heart rate (HR), systolic arterial pressure (SBP), diastolic arterial pressure (DBP), mean arterial pressure (MAP) and peripheral oxygen saturation (SpO_2) were obtained before admission to the operating room, before and after induction, after intubation, at the 1st, 3rd, 5th, 10th, 20th, 30th, 45th, 60th, 75th, 90th, 105th, and 120th minutes intraoperative, and after extubation.

Evaluation of ECG and Holter monitoring records were performed by a cardiologist who had no knowledge of the patients' assigned group. The QT interval was measured from the beginning of the QRS complex until the end of the T wave. The QT interval (QTc) corrected according to heart rate was measured using the Bazett formula ($QTc = QT / \sqrt{RR(sec)}$). The difference between the longest and shortest QT interval obtained from the standard 12 derivation was calculated as QT dispersion (QTd), whereas that between the corrected QT intervals was calculated as QTc dispersion (QTcd). The Holter monitor records were evaluated according to ventricular premature systole (VPS), atrial premature systole (APS), pause duration (Pause), and heart rate. Ventricular arrhythmias were classified according to Lown's criteria: Grade 0, No ventricular premature beat; Grade 1, Ventricular premature beat < 30 /hour; Grade 2, Ventricular premature beat > 30 /hour; Grade 3, Multifocal ventricular premature beats; Grade 4a, Couplet ventricular premature beat (two consecutive ventricular premature beats); Grade 4b, nonsustained (3 or more consecutive ventricular premature beats) or sustained (Ventricular premature beats lasting for more than 30 seconds).

2.1. Statistics

Data obtained during the study were coded and computerized using SPSS for Windows 10.0. The Pearson X^2 test was used for cross tables, the Mann-Whitney U test to compare the two independent groups. The comparison of three or more repeated measurements for dependent groups was performed using the Variance Analysis tests. A $p < 0.05$ value was considered statistically significant in all tests.

3. Results

There was no difference between the groups with respect to patient demography, anesthesia, and duration of surgery (Table 1).

Table 1. Demographic data, duration of anesthesia and duration of surgery.

	Group 1 (n=20)	Group 2 (n=20)
Age (year)	36.55 ± 9.88	32.95 ± 9.65
(Range)	(18-54)	(18-51)
Weight (kg)	72.50 ± 13.80	66.45 ± 12.63
(Range)	(50-90)	(48-85)
Gender (M/F)	13/7	11/9
Duration of anesthesia (minute)	94.00 ± 39.88	95.75 ± 37.91
(Range)	(25-180)	(45-160)
Duration of surgery (minute)	77.90 ± 40.95	74.50 ± 32.72
(Range)	(15-150)	(35-125)

Figure 1. Comparison of mean arterial pressure between the groups (Mean ± SD). (T1: preoperative, T2: before induction, T3: after induction, T4: after intubation, T5: intraoperative 1st min, T6: intraoperative 3rd min, T7: intraoperative 5th min, T8: intraoperative 10th min, T9: intraoperative 20th min, T10: intraoperative 30th min, T11: intraoperative 45th min, T12: intraoperative 60th min, T13: intraoperative 75th min, T14: intraoperative 90th min, T15: intraoperative 105th min, T16: intraoperative 120th min, T17: after extubation). * p<0.05.

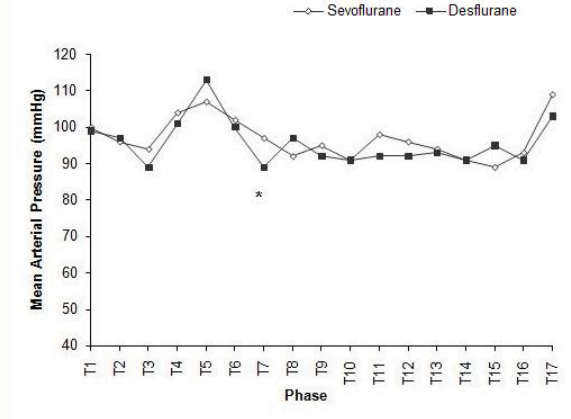
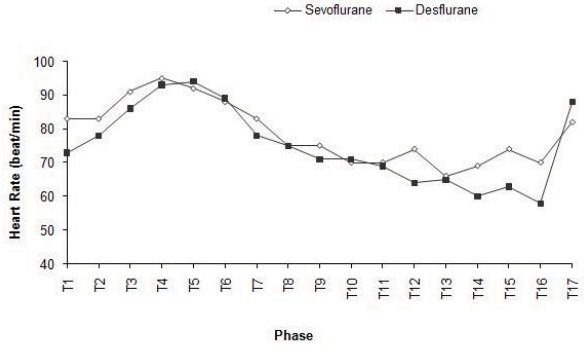


Figure 2. Comparison of mean heart rates between the groups (Mean ± SD). (T1: preoperative, T2: before induction, T3: after induction, T4: after intubation, T5: intraoperative 1st min, T6: intraoperative 3rd min, T7: intraoperative 5th min, T8: intraoperative 10th min, T9: intraoperative 20th min, T10: intraoperative 30th min, T11: intraoperative 45th min, T12: intraoperative 60th min, T13: intraoperative 75th min, T14: intraoperative 90th min, T15: intraoperative 105th min, T16: intraoperative 120th min, T17: after extubation).



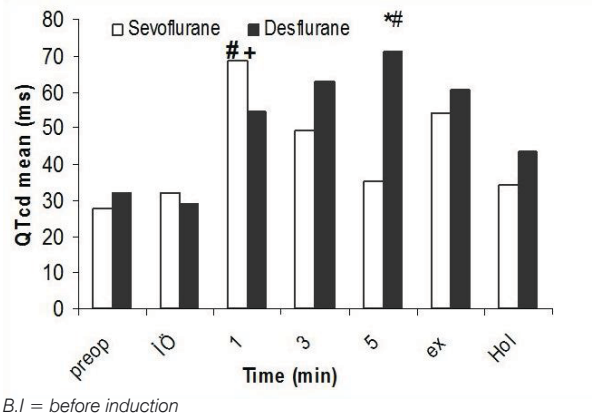
The MAP values at the following periods in both groups are shown in Figure 1. Comparison of both groups demonstrated that there was no statistically significant difference between the two groups with respect to HR values (p>0.05) (Figure 2). The QTcd value in the sevoflurane group at the 1st, and in the desflurane group at the 5th minute, were found to be significantly high with respect to preoperative and pre-induction values. In the sevoflurane group, the QTcd value at the 1st minute was also found to be significantly high with respect to the QTcd value at the 5th minute and after Holter ($p < 0.05$) (Figure 3).

Data obtained from Holter records during the pre- and postoperative periods demonstrated that ventricular arrhythmia was significantly increased in the postoperative period in the desflurane group (15% and 70%, respectively; $p < 0.01$). A weak correlation between the increase in QT dispersion and the occurrence of arrhythmia was identified in the desflurane group (r = 0.31). Nonsustained ventricular tachycardia and sustained ventricular tachycardia, considered to be clinically serious arrhythmias, were not observed in either group.

4. Discussion

Prolonged QT interval is known to cause life-threatening arrhythmias and sudden cardiac death during anesthesia [8]. Therefore, it is very important to carefully examine the ECGs of patients having a congenital or acquired prolonged QT syndrome who are to be anesthetized. The ECGs of these patients also inform the choice of appropriate anesthetic agents to prevent possible rhythm disorders. Studies have been conducted to investigate the effect of volatile anesthetic agents on QT interval and dispersion. Prolongations of QT interval (QTc > 440 milliseconds) are disorders of the cardiac autonomic nervous system that cause ventricular arrhythmias and also decrease the ventricular fibrillation threshold [9]. Changes in plasma catecholamine levels are also known to affect the QTc interval and mean arterial pressures [10].

Figure 3. Comparison of mean QTc dispersion between the groups (Mean ± SD).



B.I = before induction
** Comparison of QTc dispersion values between the groups p<0.05*
 # Comparison of QTc dispersion values at the 1st min. with respect to preoperative values intragroup 1 and at the 5th min. with respect to preoperative values intragroup 2; p<0.05
+ Comparison of QTc dispersion values 1st min. with respect to post Holter values p < 0.05
(Preop: preoperative, I.O: before induction, 1: 1st minutes after intraoperative MAC 1, 3: 3rd minute after intraoperative MAC 1, 5: 5th minutes after intraoperative MAC 1, ex: extubation moment, Hol: Postoperative 24th hour when Holter is removed).

Guler et al. have investigated the effects of halothane and sevoflurane on the cardiovascular system and QT dispersion. These authors observed that halothane and sevoflurane caused a significant increase in QT dispersion without prolonging QT interval [11]. In a study conducted by Kleinsasser et al, healthy female patients who were to undergo elective gynecologic surgery were divided into two groups. In the first group, anesthesia was performed using a face mask, and with addition of a 2.5% concentration of sevoflurane into 100% O_2; in the second group, anesthesia was performed by administering 30% oxygen with 20 mL/hour propofol infusion following a 2.5 mg/kg induction dose. Comparing the basal values of QT and QTc intervals of patients before induction with the measurements after 20 minutes of induction, no arrhythmia was observed to have developed in the patients, and the QTc interval did not exceed 440 milliseconds; however, it was suggested that sevoflurane significantly prolonged the QTc interval [12]. On the other hand, Gurkan et al reported that halothane and sevoflurane used for induction in pediatric patients caused various levels of abnormalities in ventricular repolarization following tracheal intubation, and that a greater increase of the QTd and QTcd values was observed in halothane following the intubation [13].

Yildirim et al compared sevoflurane, isoflurane, and desflurane with respect to QT interval and dispersion; they found a significant increase both in QT interval and QT dispersion with respect to the pre-induction period 10 minutes after sevoflurane attained its effective concentration. In the desflurane group, the increase in QT interval and dispersion began right after induction, and this effect continued until the 3rd and 10th minutes after desflurane attained its effective concentration. However, no difference was observed between the groups with respect to QT interval and dispersion [14]. The desflurane and sevoflurane used in our study statistically significantly prolonged the QTc values of all periods, other than values after Holter with respect to the basal value of QTc before anesthesia. However, in the desflurane group, the 5th minute maximum QTc was found to be statistically significantly longer than that in the sevoflurane group.

In the present study, a significant increase was observed both in QT interval and QT dispersion 1 minute after sevoflurane attained its effective concentration with respect to pre-induction. Prolongation in the QT interval continued to decrease thereafter; however, the QT dispersion lost significance with respect to the pre-induction period. In the desflurane group, prolongation in the QT interval began 1 minute after desflurane attained its effective concentration, and a significant increase was observed in both the QT interval and QT dispersion at the 5th minute with respect to the pre-induction period.

Cardiac arrhythmia is one of the important side effects of anesthetic agents. Halothane, one of the most investigated anesthetics with respect to cardiac arrhythmias, is known to cause ventricular arrhythmia. Comparison of halothane to sevoflurane demonstrated that halothane caused more obvious ventricular arrhythmia than sevoflurane [16]. Results from many case reports have shown that sevoflurane causes advanced arrhythmias, such as Torsade de Pointes and ventricular fibrillation, in several congenital diseases and in patients with congenital prolonged QT syndrome [17-19].

In a study where sevoflurane and desflurane were compared in pediatric patients with respect to cardiac arrhythmia and QT interval, a marked prolongation of QT interval was identified in the desflurane group. However, no difference in arrhythmia was observed [20]. Desflurane has been reported to cause ventricular arrhythmia by activating the sympathetic nervous system [21-23]. In the present study, we demonstrated a statistically significant increase in ventricular arrhythmia in the desflurane group during the first 24 hours after induction. This result showed that more careful follow-up was needed for arrhythmia during the first 24 hours after induction in the desflurane group as compared with the sevoflurane group.

Our study has several limitations. First, in this study, the number of patients is very small. The other limitation is that patients should have been monitored for cardiac arrhythmias after the first 24 hours.

5. Conclusion

Desflurane increases cardiac arrhythmias and gives rise to an increase in QTcd. Although the use of beta blockers is recommended before anesthesia in patients with prolonged QT syndrome, more attention should be paid to the use of volatile anesthetic agents with regard to sinusal pause, since sinusal pause is also increased in this group.

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