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Original Contribution

Effects of remifentanil, nitroglycerin, and sevoflurane on the corrected QT and Tp-e intervals during controlled hypotensive anesthesia☆

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Abstract

Study objective: Controlled hypotension is a preferred method in various surgical operations, but limited data are available for the effects of drug combinations that are used to ensure the desired level of hypotension on cardiac repolarization.
Design: Randomized, prospective, double-blinded study.
Patients: The study comprised 65 patients undergoing septorhinoplasty surgery under general anesthesia.
Interventions: Group S received sevoflurane inhalation alone, group R received sevoflurane and remifentanil, and group N received sevoflurane and nitroglycerine in a way that a mean arterial pressure of 60 ± 5 mm Hg was achieved.
Measurements: Electrocardiogram was performed before induction (T1), 30 minutes after induction (T2), and 5 minutes after extubation (T3). Corrected QT (QTc), QT dispersion (QTd), and corrected Tp-e (Tp-ec) intervals and Tp-e/corrected QT (Tp-e/QTc) ratio were calculated.
Main results: QTc prolongation was observed at T2 and T3 in all groups, but only QTc prolongation at T2 was statistically significant in group S ($P > .05$). Significant prolongation of QTd interval at T2 and T3 was observed in group S ($P < .05$). In all groups, Tp-ec decreased at T2. However Tp-ec decrease was not statistically significant in group S ($P = .103$) and group R ($P = .058$). Tp-e/QTc was significantly decreased on T2 in all 3 groups, and it was returned to baseline at T3 ($P < .05$).
Conclusion: The present study demonstrated that none of the 3 hypotensive anesthesia methods has an overall negative effect on Tp-e and Tp-e/QTc. Therefore, we conclude that all 3 methods can be used safely in terms of proarrhythmic risk, but increased sevoflurane consumption may require more attention due to significant prolongation of QTc and QTd.

1. Introduction

It is known for a long time that various anesthetic agents have arrhythmogenic potential because they affect ventricular repolarization [1]. However, there are contradictory reports on

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the effects of anesthetic agents and methods on perioperative ventricular repolarization. Ventricular repolarization disorder triggered by anesthesia poses risk for malignant ventricular arrhythmia such as torsade de pointes (TdP) and manifests itself with prolonged QT interval and various T-wave alterations on the electrocardiogram (ECG). TdP may either end spontaneously or rapidly turn into ventricular fibrillation. Symptoms include palpitation, syncope, seizure, and sudden cardiac death.

Many external factors influence repolarization due to various effects on ion channels on myocytes. Anesthetic agents, methods used in clinical anesthesia practice, and the medications of patients may influence the QT interval [2]. QT interval, corrected QT (QTc) interval, QT dispersion (QTd), T-wave peak-to-end interval (Tp-e), and Tp-e/QTc ratio are ECG indicators of ventricular arrhythmogenesis [3]. Transmural dispersion of repolarization (RTD), which is known as Tp-e on ECG, is one of the most important markers of TdP [4]. This period is well known as the most sensitive time interval for prediction of the development of TdP [5]. The epicardial cells in the myocardium are repolarized first, whereas midmyocardial (M) cells are repolarized last. The T-wave peak coincides with the completion of epicardial repolarization [6], and repolarization of the M cells coincides with the end of the T wave. As compared with the other ventricular myocardial cells, M cell action potential might be significantly prolonged because of certain factors including drugs. Consequently, the heterogeneity of this action potential phase between the cells leads to the formation of regions with various refractivity. Early after depolarizations, which occur accordingly, create reentry cycles between these regions and develop TdP and ventricular fibrillation by forming R-on-T phenomenon [7].

Hypotensive anesthesia is an anesthesia method created by deliberately lowering the blood pressure with various agents with a caution of avoiding hypoperfusion. This method is used to reduce blood loss and improve the quality of surgical field. Anesthetic agents are frequently used in combination with opioids or hypotensive agents in hypotensive anesthesia. Various studies have investigated the torsadogenic potential of sevoflurane. Studies and case reports indicating significant QT, QTc, and QTd prolongation during sevoflurane anesthesia suggest that it has some arrhythmogenic potential [8–11]. Despite limited data about the effect of using remifentanil in the maintenance of hypotensive anesthesia on arrhythmogenic markers, it was found that the addition of remifentanil to sevoflurane in the induction of anesthesia has no electrophysiological effect in the short-term period [12].

There are limited data about decrease in coronary blood flow and cardiac repolarization abnormalities during controlled hypotension. In the present study, our objective was to investigate the effects of using sevoflurane alone and in combination with remifentanil or nitroglycerine on QTc interval and other parameters of repolarization in patients undergoing septorhinoplasty surgery under controlled hypotensive anesthesia.

2. Methods

We enrolled 65 American Society of Anesthesiologists I-II patients who were scheduled for septorhinoplastic surgery under general anesthesia between September 2013 and April 2014. Ages of patients ranged between 18 and 65 years. The study was approved by the local ethics committee, and written informed consent was obtained from all patients.

The exclusion criteria for the patients included those who refused to participate in the study, patients with known allergy to study drugs, and those with known structural or arrhythmic cardiac disease. Moreover, patients with ventricular conduction disturbances on the baseline ECG or a corrected QT interval of >450 milliseconds in male patients and >460 milliseconds in female patients on the baseline ECG, those with drug use that has potential to change QT interval, and patients with electrolyte disorder were also excluded from the study.

Sedation for premedication was not performed in any of the patients. All study data were collected in the morning. The patients were noninvasively monitored for blood pressure after their admission to the operation room. Initial 12-lead ECG was performed before induction and was called T1. Places of ECG electrodes were not changed over the course of the surgery. Intravenous line was opened, and 0.9% NaCl infusion was started at a dose of 10 mL/(kg h) in the first hour and 5 mL/(kg h) thereafter. For preoxygenation, 100% O_2 was administered for 3 minutes, and all patients received 2-2.5 mg/kg propofol, 1 mg/kg lidocaine, 1 μg/kg fentanyl, and 0.8 mg/kg rocuronium for induction. After providing adequate depth of anesthesia, the patients were intubated. Maintenance of anesthesia was provided using sevoflurane (an inspiratory concentration of 2%-3%) and a mixture of 50% O_2-N_2O. Patients were randomly divided into 3 groups. The first group (n = 22) received sevoflurane inhalation alone (group S), the second group (n = 21) received sevoflurane inhalation and remifentanil infusion (0.5 µg/kg bolus in 60 seconds and then 0.1-0.5 µg/(kg min) infusion) (group R), and the third group (n = 20) received sevoflurane inhalation and nitroglycerine infusion (0.5-2 µg/[kg min]) (group N), aiming for a mean arterial pressure (MAP) of 60 ± 5 mm Hg. No local anesthetic drug was administered to the patients. The dose of sevoflurane was increased to achieve targeted level of hypotension in the first group. The amounts of sevoflurane, remifentanil, and nitroglycerine used over the course of surgery were recorded. Intraoperative ECGs of the patients were performed after stable hypotension level was achieved (T2). Heart rate (HR) and MAP of all patients within target levels of controlled hypotension were recorded at 10-minute intervals in the first hour and then at 15-minute intervals until the end of surgery. At the end of surgery, the last ECGs (T3) of the patients were performed 5 minutes after extubation. ECGs were performed using Philips Pagewriter (Pagewriter Trim II, Philips, Netherlands) device at a speed of 25 mm/s and with amplitude of 10 mm/mV. ECGs were transferred to the digital media, and measurements were done manually at a magnification of 400% by an experienced