Title: PROLONGED QT INTERVALS INDUCED BY ENFLURANE, ISOFLURANE AND HALOTHANE IN CHRONICALLY INSTRUMENTED DOGS

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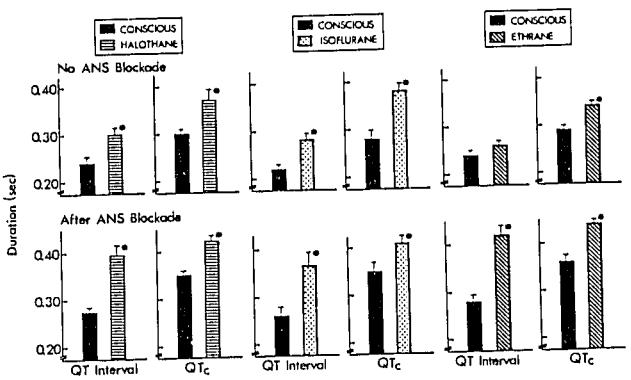
Introduction. The QT interval measured from the beginning of the QRS complex to the end of the T wave, represents the total duration of ventricular systole, including myocardial depolarization and repolarization. This interval is rate-dependent and must be corrected for changes in basal heart rate for comparison (the corrected QT expressed as QT_C). Prolongation of the QT_C has been shown to increase the vulnerable period (relative refractory period) of the heart to arrhythmias as well as to increase the incidence of ventricular premature beats. Both of these phenomena have been demonstrated to potentiate the development of reentrant arrhythmias, such as ventricular fibrillation, leading to syncope or sudden cardiac death (1). The direct effects of the volatile anesthetics on the QT_C have not been systematically examined. The present investigation was designed to evaluate the direct electrocardiographic (EKG) and hemodynamic effects of halothane (H), isoflurane (I) and enflurane (E) in the chronically instrumented dog. Because the autonomic nervous system (ANS) may play an important role in prolongation of the QT interval, anesthesia was administered with and without concomitant ANS blockade.

Methods. Mongrel dogs were instrumented with catheters for measurement of aortic blood pressure (BP), Doppler flow transducers for measurement of coronary blood flow velocity and a left ventricular (LV) miniature micromanometer for measurement of LV systolic and end diastolic pressures and dP/dt, an index of LV global contractility. EKG leads (corresponding to limb lead II) were sutured to the internal thoracic wall. Dogs were allowed to recover for 10 days prior to study. Six experimental groups were completed (N = 6-11 each). In 3 separate groups, after obtaining conscious control measurements, the EKG and hemodynamic effects of H (2%), I (2%) or E (4%) in oxygen were studied. Concentrations of each anesthetic were selected to provide a 20-30 mm Hg decrease in mean arterial pressure. In an additional 3 groups of experiments, EKG and hemodynamic effects of the 3 anesthetics were also determined in dogs with ANS blockade produced by propranolol (2.0 mg/kg), methylatropine (3.0 mg/kg), hexamethonium (20.0 mg/kg), and phentolamine (2.0 mg/kg with a 0.25 mg/kg/hr infusion). Arterial blood gas tensions and anesthetic concentrations were determined in all groups. All data were compared to control via ANOVA followed by Dunnett's t-test and considered significant (*) when p 0.05.

Results. In all groups, no change in the QRS duration was observed. While I and E had no effect, H significantly prolonged the PR interval. In the absence of ANS blockade, H and I significantly prolonged the QT interval (0.24 ± 0.01 to 0.30 ± 0.01 and 0.22 ± 0.01 to 0.28 ± 0.01 seconds, respectively) while E produced no change in ventricular repolarization (0.24 ± 0.01 to 0.26 ± 0.01 seconds) (Figure 1). All of the anesthetics increased the QT interval corrected for changes in basal heart rate (QT_C), and all agents decreased BP and dP/dt. Following ANS blockade, H, I and E significantly increased the QT interval and QT_C.

Discussion. The QRS interval was unchanged by volatile anesthesia, indicating that prolongation of QT_C reflected delayed repolarization. Since prolonged QT_C may represent imbalanced cardiac sympathetic activity (2), pharmacological blockade of sympathetic and parasympathetic influences was utilized to observe the direct effects of H, I and E on QT_C. The results demonstrate that ventricular repolarization is directly altered by the volatile anesthetics independent of changes in ANS tone. Whether or not such effects are additive with other congenital or acquired forms of QT_C prolongation has yet to be examined. The present results indicate that caution should be utilized during the administration of volatile anesthetics to patients with abnormalities of the QT interval.



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