# Effects of anesthesia on the heart

October 27 2008

Researchers at Rhode Island Hospital have created the first animal model that can reveal the side effects of anesthetic agents (the substances used to block pain during surgery) in individuals genetically predisposed to sudden cardiac death. The researchers also found that some anesthetic agents may trigger arrhythmias. The study appears in an upcoming issue of the *American Journal of Physiology – Heart Circulation Physiology* and is currently available online.

Researchers know that genetic mutations can predispose individuals to arrhythmia and/or sudden cardiac death (SCD), a leading cause of death in the United States. Between one in 2,500 and one in 5,000 individuals are born with mutations that cause long QT syndrome (LQTS), a disorder of the heart's electric system, and a determining factor in the development of arrhythmia and/or SCD. Ninety percent of the known mutations cause loss of function of ion channels responsible for LQTS types 1 and 2 (LQT1 and LQT2).

LQTS leads to a prolonged QT interval on electrocardiograms. The QT interval refers to the time it takes the chambers of the heart to "repolarize" themselves so that the heart is ready for another contraction cycle. When this timeframe is lengthened, it is associated with triggering irregular arrhythmia that can cause sudden cardiac arrest.

Earlier this year, researchers at the Cardiovascular Research Center at Rhode Island Hospital developed a first-of-its-kind genetic animal model to study arrhythmia and SCD that mirrors what happens in individuals who have mutations of the LQT1 or LQT2 genes. With the rising

interest in pharmacogenomics (the study of the effect of an individual's genotype on the body's potential response to medications) the researchers have taken the model one step further and have developed what they believe is the first model to test the safety and efficacy of drugs such as anesthetics when these genetic mutations are present.

Senior author Gideon Koren, MD, director of the Cardiovascular Research Center at Rhode Island Hospital and a professor of medicine at the Warren Alpert Medical School of Brown University, says, "We believe the animal model we have created is the first to be able to accurately predict the effects of various anesthetic agents when LQTS is present. Also, our findings indicate that some anesthetic agents can trigger arrhythmias."

The researchers looked at five common anesthetic agents, including isoflurane, thiopental, midazolam, propofol and the veterinary anesthetic ketamine. Varied effects were noted with each anesthetic in the different models. For instance, isoflurane resulted in a prolonged QT interval in LQT2 but not in LQT1 models, whereas thiopental prolonged the QT interval in both LQT1 and LQT2, though the increase was less pronounced in LQT1. Midazolam prolonged the QT duration in both LQT1 and LQT2 but not in controls, while propofol significantly increased the QT interval in both LQT1 and LQT2 models and the control group.

During the monitoring periods under anesthesia, signs of altered repolarization and arrhythmias were noted only in LQT2 models. Multiple premature ventricular contractions, which can have a marked effect in humans, occurred in many LQT2 models under midazolam, ketamine or thiopental. Also noted is that isoflurane and propofol were especially proarrhythmic in LQT2 models and led to sudden cardiac death in a total of three LQT2 out of nine LQT2 models.

Koren concludes, "We anticipate a great deal more in the way of findings from the development of this model. For now, this study should serve as a reminder to anesthesiologists that an ECG prior to surgery must be carefully studied." He adds, "Further, we would recommend that for those individuals whose ECG appears borderline for LQTS, genotyping may be advisable in order to determine if there is a mutation of the LQT1 or LQT2 genes before selecting anesthetic agents."

Source: Lifespan