Title: DO ISOFLURANE AND HALOTHANE ATTENUATE CORONARY ARTERY CONSTRICTION IN PIGS?

Authors: T. M. Witzeling, M.D.; J. C. Sill, M.B.B.S.; J. M. Hughes, M.D.; M. Nugent, M.D.; G. A. Blaise, M.D.

Affiliation: Department of Anesthesiology, Mayo Clinic, Rochester, MN 55905. Supported by the B. B. Sankey Achievement Award from the International Anesthesia Research Society.

Introduction. Isoflurane and halothane are predictable and safe anesthetics. In experimental animals and in human beings they protect the ischemic heart by depressing myocardial oxygen consumption. However, it has become apparent that myocardial ischemia is not only caused by elevated myoardial oxygen consumption but also by acute decreases in myocardial oxygen supply. Epicardial coronary artery constriction superimposed upon atherosclerosis is thought to be the mechanism. This constriction is believed to contribute to exertional angina and may precipitate or exacerbate coronary thrombosis in myocardial infarction. Volatile anesthetics are vasoactive drugs. It is unknown whether or not they are sufficiently potent to inhibit constriction of coronary arteries. Our aim was to determine whether or not isoflurane and halothane would attenuate constriction induced by intracoronary serotonin infusion. Serotonin was used as it has been implicated in human coronary constriction. In order to mimic human atherosclerosis and to test the role of the endothelium, both normal animals and animals with damaged coronary endothelium were studied. Finally, in order to provide comparison to a known epicardial coronary dilator with definite therapeutic effects, intravenous nitroglycerin was also tested.

Methods. Fourteen pigs were studied. Using fluoroscopy, a catheter was placed in the left coronary ostium and was used to inject radiopaque dye. Through it a smaller catheter was advanced 1 cm into the left anterior descending coronary artery and was used to infuse serotonin. Effects of isoflurane, halothane, and nitroglycerin upon serotonin mediated constriction were assessed using coronary angiography. Vessel luminal diameters were measured using a computer based image analysis system. Diameters were obtained every 1 mm along the vessel length. In some animals, coronary endothelium was damaged using a balloon catheter. Completeness of endothelium removal and integrity of underlying smooth muscle were assessed histologically.

Results. Stable coronary constriction was produced by constant infusion of serotonin. Isoflurane, halothane, and nitroglycerin were then given. Effects in pigs with normal arteries are shown in Figure 1. Both anesthetics and nitroglycerin produced coronary dilatation. In another experiment, also in pigs with normal vessels, three vasoconstricting doses of serotonin were given. Figure 2 shows vasoconstrictor effects without anesthetics and attenuated vasoconstriction following isoflurane and halothane administration. Preliminary results following endothelial damage indicate volatile anesthetics continue to vasodilate.

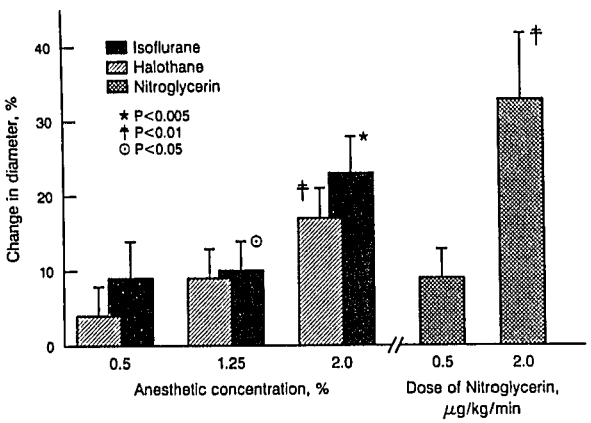

Fig. 1: Effects of isoflurane, halothane, and nitroglycerin upon coronary constriction established by constant serotonin infusion.

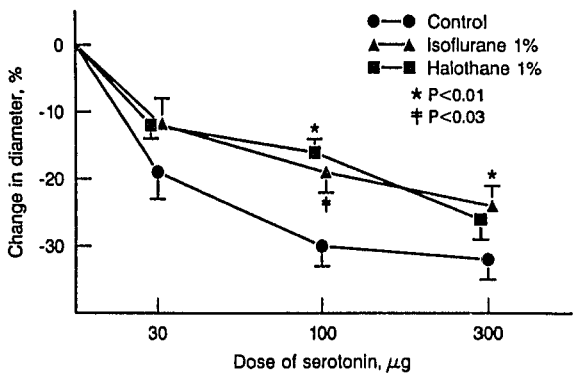

Fig. 2: Effects of serotonin on vessel diameter in absence of volatile anesthetics, and in the presence of 1% isoflurane and 1% halothane.

Discussion. Isoflurane and halothane attenuate serotonin induced coronary artery constriction in pigs. Preliminary data suggests this effect persists despite damage to the endothelium. Surprisingly, the degree of anesthetic-induced dilatation is similar to that produced by low dose intravenous nitroglycerin. The mechanism of these effects is unknown. If similar effects occur in humans with coronary disease, then it is possible that volatile anesthetics could induce small degrees of dilatation at coronary stenoses and in this way improve blood flow to the heart.