TITLE: PROPOFOL, THIOPENTAL AND CONTRACTILE RESPONSES IN ISOLATED PIG CORONARY ARTERIES AND CULTURED VASCULAR SMOOTH MUSCLE CELLS

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Little is known concerning the effects of propofol on coronary arteries. Barbiturates have been shown to contract quiescent dog coronary arteries. The purpose of this study was to determine the effects of propofol and thiopental on (a) quiescent pig coronary artery tone; (b) contractile responses evoked by serotonin, acetylcholine, prostaglandin $F_{2\alpha}$ and histamine; (c) relaxation responses to bradykinin; (d) changes in cytosolic Ca^{2+} evoked by vasopressin in cultured vascular smooth muscle cells.

(a) Coronary artery rings ± endothelium were studied in organ chambers and changes in tension induced by propofol and thiopental were measured. (b) Contractions evoked by cumulative increasing concentrations of the four contractile agonists were studied with and without 10^{-4}M propofol or 10^{-4}M thiopental. (c) Relaxations induced by bradykinin were measured with and without the anesthetics. (d) Cells (A10) were loaded with the fluorescent indicator indo-1/AM. Cytosolic Ca^{2+} responses to vasopressin 10^{-7}M were measured in individual cells at 400-800 cells.sec^{-1} in the presence and absence of the anesthetics using a flow cytometer.

Results: (a) propofol caused slight relaxation while thiopental causes slight contraction of coronary rings (Fig. 1); (b) both anesthetics attenuated contractions evoked by serotonin (Fig. 2) but had minimal effects on contractions of other agonists; (c) neither anesthetic altered endothelium-dependent relaxation; (d) neither anesthetic had a marked effect on cytosolic Ca^{2+} transients evoked by vasopressin.

The results suggest that propofol and thiopental differ in their effects on quiescent pig coronary arteries. They both have specific effects on agonist induced responses.

Figure 1

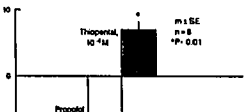
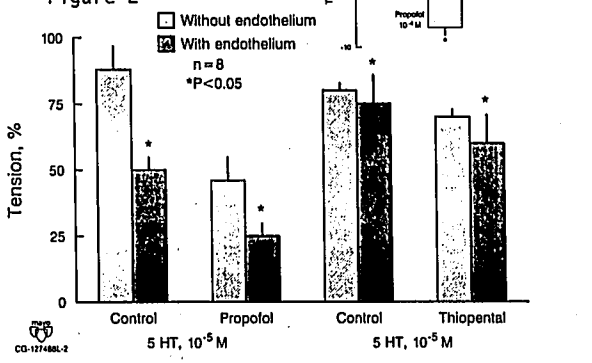


Figure 2



A584

TITLE: ISOFLURANE, HALOTHANE AND RESPONSES TO ENDOTHELIN IN PIG CORONARY ARTERIES AND CULTURED VASCULAR SMOOTH MUSCLE CELLS

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Endothelin is a potent vasoconstrictor synthesized by the endothelium. In animals it causes sustained coronary, renal and cerebral vasoconstriction and extension of myocardial infarction and in humans is increased in the plasma during myocardial infarction. The purpose of this study was to determine if isoflurane and halothane (a) inhibit contractions evoked by endothelin in isolated pig coronary arteries; (b) attenuate cytosolic Ca^{2+} transients evoked by endothelin in cultured vascular smooth muscle cells, measured using the fluorescent indicator indo-1.

Coronary artery rings with and without endothelium were studied in organ chambers and changes in tension induced by endothelin 10^{-12}M to 10^{-8}M were measured in the presence and absence of isoflurane 2% and halothane 2%. In addition, stable contractions were induced by endothelin 10^{-8}M and 0.5, 1.0, 1.5, 2.0, 2.5% isoflurane or halothane administered. Effects of nitroprusside 10^{-9}M to 10^{-6}M were also tested. (b) Cells (A10) were loaded with Indo-1/AM. Cytosolic Ca^{2+} responses to endothelin 10^{-9}M were measured in individual cells at 400-800 cells.sec^{-1} with and without 1.5% anesthetics, using a flow cytometer.

Results indicate that: (a) Endothelin caused concentration-dependent contractions that were only minimally inhibited by isoflurane 2% and halothane 2%. Stable contractions were also only minimally depressed by the anesthetics. In contrast, nitroprusside 10^{-6}M induced 91±2% relaxation ($p<0.01$). (b) Both anesthetics decreased the Ca^{2+} signal evoked by endothelin 10^{-9}M, however, the magnitude of the inhibition was small (Figure).

The results suggest that although increase in cytosolic Ca^{2+} is attenuated by the anesthetics, their ultimate effect on contraction is small. Endothelin may evoke contractions by a mechanism that is predominantly resistant to the anesthetics.