

Title: DISSIMILAR EFFECTS OF ISOFLURANE VERSUS DIPYRIDAMOLE ON MYOCARDIUM SUPPLIED BY A CHRONICALLY NARROWED CORONARY ARTERY IN THE DOG

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**Introduction.** Isoflurane is a coronary vasodilator and, therefore, may contribute to the development of myocardial ischemia. On the other hand, it can be hypothesized that by reducing myocardial metabolic demands, isoflurane could decrease the extent of myocardial injury. The goal of this investigation was to determine the effects of isoflurane versus near maximum coronary vasodilation with dipyridamole on the contractile function of myocardium supplied by a chronically narrowed coronary artery.

**Methods.** Doppler ultrasonic flow transducers and hydraulic cuff occluders were placed around the circumflex coronary arteries, few mm below the edge of the left atrial appendage, in fourteen healthy, trained mongrel dogs. In nine animals a ligature was passed beneath each freed coronary artery, just distal to the flow transducers. The ligature was tied around the vessel and a 20-gauge needle along its side. The needle was immediately withdrawn allowing some flow in the circumflex coronary artery. Pairs of miniature ultrasonic transducers were placed intramyocardially, parallel to the muscle fibers in normal and ischemic zones. Experiments were conducted 2-4 weeks after operation. While the conscious, unsedated dogs rested quietly, absence of reactive hyperemia was either confirmed or the circumflex coronary artery was gradually constricted until reactive hyperemia disappeared suggesting exhaustion of the vasodilator reserve. The effects of isoflurane (1%, 2% and 3% inspired concentration) were then studied with ventilation held constant ( $O_2, N_2, FiO_2 = 0.25$ ). Responses were compared to control by analysis of variance.

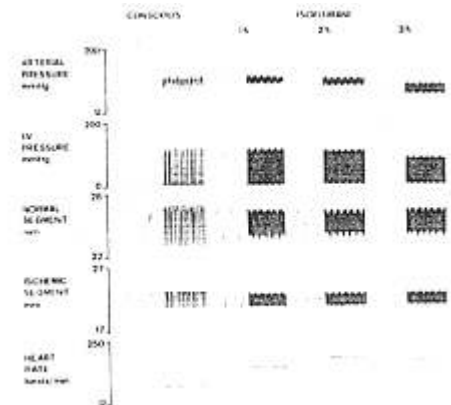
**Results.** Isoflurane increased heart rate (HR) but decreased left ventricular (LV)-end-diastolic pressure (EDP), end-diastolic segment length (EDSL), LV-systolic pressure (SP), LV-dP/dt and mean arterial pressure (MAP). No significant difference in the contractile function of the normal (NS) and ischemic (IS) muscle segments was observed, i.e., the relative decreases in segment shortening (SS) were similar in the two areas. However, dipyridamole (0.6 mg/kg iv) which increased coronary flow to normal zones by  $483 \pm 17\%$  caused striking ischemic myocardial dysfunction.

**Discussion.** In dogs with a chronically narrowed coronary artery isoflurane caused the expected depression of the myocardial contractile state with a decrease in LV-systolic performance but, in contrast to

dipyridamole, neither exaggerated nor permanent dysfunction of ischemic myocardium was detected. Thus, the present study is not indicative of a major functional significance of coronary steal during isoflurane anesthesia in the dog.

|                   | CONSCIOUS    | ISOFLURANE     |                |                |
|-------------------|--------------|----------------|----------------|----------------|
|                   |              | 1%             | 2%             | 3%             |
| NS-EDSL (mm)      | 25.0<br>±1.8 | 23.6*<br>±1.4  | 23.4*<br>±1.3  | 23.9*<br>±1.5  |
| NS-SS (mm)        | 4.7<br>±0.6  | 3.4*<br>±0.3   | 2.7**<br>±0.2  | 2.3**<br>±0.2  |
| IS-EDSL (mm)      | 23.8<br>±1.0 | 23.0**<br>±1.0 | 22.9**<br>±0.9 | 23.3**<br>±1.0 |
| IS-SS (mm)        | 2.7<br>±0.3  | 2.1**<br>±0.3  | 1.9**<br>±0.2  | 1.4**<br>±0.2  |
| LV-EDP (mmHg)     | 13<br>±1     | 8**<br>±1      | 9**<br>±1      | 12<br>±1       |
| LV-SP (mmHg)      | 118<br>±3    | 98**<br>±3     | 86**<br>±5     | 77**<br>±4     |
| LV-dP/dt (mmHg/s) | 2663<br>±123 | 1936**<br>±108 | 1682**<br>±100 | 1358**<br>±68  |
| MAP (mmHg)        | 101<br>±2    | 87**<br>±5     | 80**<br>±5     | 70**<br>±4     |
| HR (bpm)          | 94<br>±2     | 128**<br>±6    | 140**<br>±7    | 138**<br>±7    |

Results from animals with chronic myocardial ischemia. Values are means  $\pm$  S.E.M. Isoflurane significantly different from conscious \*  $p < 0.05$ , \*\*  $p < 0.01$ .



Typical response to isoflurane in an animal with chronic myocardial ischemia.