

**Title: GLOBAL ISCHEMIA AND REPERFUSION IN VITRO - EFFECTS OF HALOTHANE ON CONTRACTILITY AND DEVELOPMENT OF DYSRHYTHMIAS**

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Volatile anesthetics have generated interest as agents which may reduce myocardial damage and dysrhythmias during ischemia and reperfusion (RP).<sup>1</sup> In isolated heart, halothane (HAL) produces a decrease in calcium accumulation following regional ischemia and RP<sup>2</sup> and dramatically improves cardiac function following global hypoxia and reoxygenation.<sup>3</sup> The purpose of this study was to examine the effects of HAL on functional recovery, incidence and duration of arrhythmias following 30 min of perfusion at reduced perfusion pressure (PP).

The guinea pig hearts (n=77) were isolated and perfused at PP (55 mmHg) with modified Krebs-Ringer solution (PO<sub>2</sub> 535 mmHg). Left ventricular pressure, heart rate (HR) and atrio-ventricular conduction time (AVCT) were measured at 10 min intervals. PO<sub>2</sub> was also measured for MVO<sub>2</sub> calculation. Hearts were divided into three groups and perfused at 0, 10 and 25% of the initial PP for 30 min. Each of these groups was subdivided into three groups and exposed to 0, 0.75 (222±10 μM) or 1.5% (510±19 μM) HAL 10 min prior to, during, and 10 minutes following HP. HP was followed by 40 min of RP at normal PP. ANOVA and Chi-square tests were performed. Data are means±SEM.

HAL decreased HR by 9 and 12% (control 215±4bpm); MVO<sub>2</sub> by 13 and 14% (control 59±9 μl/min/g); SLVP by 25 and 51% (control 96±5 mmHg), during 0.75 and 1.5%, respectively. During HP, SLVP and HR decreased and AVCT progressively increased; AV block and/or atrial and ventricular dysrhythmias occurred in all hearts during 0 and 10% and in some hearts during 25% PP. Predominant

dysrhythmias during HP were 2° and 3° AV block and bradycardias which progressed to atrial and/or ventricular arrest during 0% PP. After HP at 0% PP 0.75% HAL decreased duration of VF, while 1.5% HAL decreased duration of VF and VT (Figure 1). Only 1.5% HAL reduced incidence of VT but not of VF. During HP at 0 and 10% hearts almost cease to contract. HAL did not influence the recovery of contractile function in these groups. Contrary to HP at 0 and 10%, HAL decreased contractility during HP at 25% and facilitated recovery of SLVP (Figure 2).

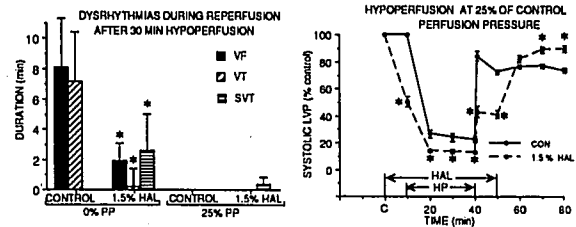


Figure 1

\* p&lt;0.05 vs Control

Figure 2

In the isolated heart, we found that 30 min of HP at PP's of 0, 10 and 25% of control does not severely limit restoration of cardiac function as compared with 30 min of hypoxia.<sup>3</sup> After discontinuation of HAL, following HP at 25 but not at 0 and 10%, SLVP was significantly higher in HAL groups than in control group, suggesting the protective effect of HAL. HAL also decreased the duration of VF during RP following 0% HP but increased the incidence of SVT. *In vitro*, HAL offers limited protection against the development and duration of some dysrhythmias and improves recovery of contractile function during RP, possibly by reducing MVO<sub>2</sub>.

**References:** 1) *Anesthesiology* 61:657, 1984  
2) *Anesthesiology* 67:197, 1987  
3) *Anesthesiology* 69:A30, 1988

## A580

**Title: DESFLURANE: HEMODYNAMIC ACTIONS COMPARED TO HALOTHANE, ISOFLURANE AND ENFLURANE IN CHRONICALLY INSTRUMENTED DOGS**

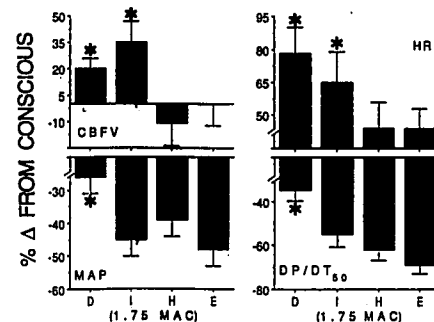
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Desflurane (D) is a new volatile anesthetic having cardiovascular actions similar to those of isoflurane as demonstrated in previous human<sup>1</sup> and swine<sup>2</sup> studies. This investigation was undertaken to examine the systemic and coronary hemodynamic actions of D compared to equianesthetic concentrations of halothane (H), isoflurane (I), and enflurane (E) in chronically instrumented dogs.

With prior approval of the Institutional Animal Care Committee, mongrel dogs (n=10) were anesthetized and instrumented for measurement of aortic blood pressure, left ventricular pressure, +dP/dt and cardiac output. Regional contractility was assessed with subendocardial ultrasonic length transducers. A Doppler flow probe was placed around the left anterior descending artery for measurement of coronary blood flow velocity. Dogs were allowed to recover from surgery for 7 days prior to experimentation. Anesthesia was induced by mask using D, H, I, or E in random fashion on separate days and hemodynamics recorded after a 30 min equilibration at 1.25 and 1.75 end tidal MAC. Arterial blood gases were maintained at conscious levels using a mixture of nitrogen and oxygen in all experiments. Changes between control and anesthetic interventions were compared by ANOVA with repeated measures followed by Bonferroni's t-test (\*p<0.05).

D and I produced significantly greater increases in heart rate than did E or H. D maintained mean arterial pressure and increased the rate pressure product to a greater degree than did H, I or E. D preserved contractile function (as indicated by +dP/dt and dP/dt<sub>50</sub>) to a greater extent than the other agents. D and I decreased cardiac output less than H or E, however, I produced a greater decline in systemic vascular resistance than did D, E or H. D and I produced similar increases in diastolic coronary blood flow velocity whereas H and E did not.



The results indicate that D possesses many hemodynamic effects which are similar to I in the chronically instrumented dog. Like I, D causes an increase in coronary blood flow. However, D preserved cardiovascular stability and contractile function to a greater degree than the other volatile anesthetics.

**References:** 1) Weiskopf *et al Anesth Analg* 70:S426, 1990; 2) Weiskopf *et al Anesthesiology* 69:303-309, 1988