

Title: DIFFERENTIAL EFFECTS OF HALOTHANE OR ENFLURANE ON HEART CELL UTILIZATION OF GLUCOSE AND FATTY ACIDS

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Introduction. Considerable interest has been generated as of late regarding the potential beneficial effects of inhalation anesthetics in the amelioration of myocardial ischemia during surgery¹. In addition, contradictory reports have appeared comparing the myocardial depressant effects of halothane with those of enflurane in both humans and animals². If it is true that inhalation anesthetics are beneficial to the ischemic myocardium it would be of interest to know if anesthetics differ in the degree to which they depress oxygen consumption. However, comparing two cardiodepressant agents such as halothane and enflurane *in vivo* is difficult since it is believed they have different effects on peripheral vascular resistance, heart rate, cardiac output, and sympathetic tone. In a recent study we reported that halothane, on an equi-dose basis, caused a significantly greater reduction in the oxygen consumption of beating heart cells in tissue culture than enflurane³. In this report we have extended these findings by measuring the effects of each anesthetic on the rate of fatty acid and glucose utilization by heart cells in culture.

Methods. Tissue cultures were prepared as follows: hearts were removed from three to five day old rats. Each heart was then transferred to trypsinization flasks. After 15 minutes of digestion with trypsin the heart cells become separated. Aliquots of this solution were then pipetted into flasks. The resultant cell count per flask was approximately eight to ten million. After about three days incubation the cells attach to the bottom of the flask and begin to beat in unison. Observation of cells during an experiment was accomplished by placing the culture plate on an inverted phase contrast microscope. A T.V. camera was adapted to the light output on the microscope. The actual image of the beating cell was then displayed on a T.V. monitor. Experiments were conducted with beating cells (200-300 times per minute). Substrate utilization rates were determined by measuring the generation of carbon-14 labelled CO₂ from either ¹⁴C-palmitic acid or ¹⁴C-glucose. Heart cell cultures were incubated with media containing ¹⁴C-glucose or ¹⁴C-palmitic acid (palmitic acid was complexed to albumin), gassed with either halothane or enflurane, and then sealed. Following 2 hrs. of incubation the ¹⁴CO₂ was purged from the culture flasks with nitrogen gas and trapped with hydroxyhyamine. Aliquots of the hydroxyhyamine were then counted by liquid scintillation. The amount of radioactivity detected was then converted to nanomoles of O₂ based on the specific activity of the of the substrates and the assumption that each substrate was 100% metabolized to CO₂. Anesthetic concentrations in the media were determined by gas chromatography.

Results. The rate of oxygen consumption per hr with glucose or palmitic acid as substrate in beating, nonanesthetized cells can be seen in Table 1. The rate of oxygen consumption with glucose or palmitic acid as substrate during halothane or enflurane anesthesia can be seen in Table 2. There was no significant difference between halothane and enflurane on the rate of glucose metabolism. However, halothane produced a significantly greater reduction in palmitic acid metabolism than enflurane.

Table 1
OXYGEN CONSUMPTION IN NONANESTHETIZED CELLS

Substrate	n moles O ₂ /mg Protein/hr
1 μ mole ¹⁴ C-Palmitic acid	246±12*
1 μ mole ¹⁴ C-Glucose	67±4

* Mean values ± SE, n = 8

Table 2
OXYGEN CONSUMPTION BY HALOTHANE OR ENFLURANE ANESTHETIZED CELLS

Substrate/Anesthetic	Anesthetic Dose			
	10 mg%	20 mg%	30 mg%	
¹⁴ C-Palmitic acid	Halothane	181±5 ⁺	133±15 ⁺	76±4 ⁺
	Enflurane	203±9	168±13	114±11
¹⁴ C-Glucose	Halothane	56±3	40± 3	33± 2
	Enflurane	52±2	44± 5	35± 4

All values represent mean n moles O₂/mg protein/hr±SE
⁺ Significantly lower than enflurane values, p<0.001; n = 12

Discussion. Results from this study confirm our previous observation that halothane is a significantly more potent metabolic depressant than enflurane³. However, since both anesthetics depress glucose metabolism to the same extent it would appear that halothane's more profound disruption of fatty acid metabolism is the reason for its' greater depressant activity.

References.

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