# Title: IN VITRO COMPARISON OF THE MYOCARDIAL DEPRESSANT EFFECTS OF ISOFLURANE AND HALOTHANE ANESTHESIA UNDER VARYING STIMULUS CONDITIONS

Authors: M.B. Neal, M.D., W.J. Wolf, M.D., B.P. Mathew, M.S., D. Bee, Ph.D.

Affiliation: Departments of Anesthesiology, Pediatrics, and Preventive Medicine and Community Health, University of Texas Medical Branch, Galveston, Texas 77550

Introduction. It has been shown that isoflurane's (ISO) in vitro negative inotropic effect diminish when myocardial muscle stimulation rates increase toward the physiological range (frequency-dependence), yet the effects of increasing muscle stimulation rates on halothane's (HAL) negative inotropic effect are unclear.[1,2] The in vitro negative inotropic effects of HAL and ISO were compared under varying stimulus conditions to determine whether these two anesthetics demonstrate differential frequency-dependence.

Methods. The myocardial depressant effects of HAL and ISO were compared using feline RV papillary muscles. In experiment 1, muscles were stimulated by field electrodes (0.2 Hz; Krebs-bicarbonate; pH 7.4; 31°C) to obtain control measures of developed tension (DT) prior to administering 4 concentrations (conc) of either ISO (0.5, 1, 2, 4%; N=5) or HAL (0.25, 0.5, 1, 2%; N=4). DT was remeasured after 20 minutes at each conc. Quadratic equations were fitted to the dose-response data obtained by least squares analysis ($R^2$ > .985 for both anesthetics). The ISO and HAL conc that decreased DT to 90, 70, 50 and 30% of control were determined to compare the relative myocardial depressant potency of ISO and HAL by linear regression analysis. In experiment 2, muscle responses at 2 similar cardiodepressant conc of ISO (1.25, 2.0%; N=6) or HAL (0.8, 1.35%; N=7) were compared at muscle stimulation frequencies of 0.05, 0.1, 0.2, 0.4, 0.8, 1 and 2 Hz. The concs were selected from the data in experiment 1 as levels that diminish muscle function to approx. 70 (low conc) and 50% (high conc) of control. After obtaining control measures of DT at all stimulation frequencies, muscles were exposed to ISO or HAL and repeat measures of DT at the different stimulation rates were obtained. Muscle responses were compared to control at each stimulation frequency, and responses at the low (70% of control) and high (50% of control) anesthetic conc were compared between the ISO and HAL groups. Data were analyzed as a 3 factor repeated measure design. Muscle responses are expressed as % of control, and represent the mean ± SD.

Results. In experiment 1, both ISO and HAL caused dose-dependent depression of DT, but HAL was significantly more depressant that ISO ($p < .001$). The myocardial depressant potency relationship by linear regression analysis was ISO conc = -.005 + 1.445 (HAL conc). In experiment 2, ISO and HAL caused comparable myocardial depression of DT at lower muscle stimulation rates (range 0.05 - 1 Hz) at both the low (ISO 1.25%; HAL 0.8%) and high (ISO 2.0%; HAL 1.35%) conc. Both ISO and HAL demonstrated some degree of frequency-dependence since their depressant effects were progressively attenuated as muscle simulation rates increased, yet at high muscle stimulation rates (2 Hz) ISO was significantly less depressant than HAL at both the low (ISO 1.25%; HAL 0.87%; p=.001) and high (ISO 2.0%; HAL 1.35%; p<.0001) conc (Figure 1 A and B).

Discussion. Both ISO and HAL demonstrate frequency-dependence since the negative inotropic effects of both agents are attenuated by increasing muscle stimulation rates, however, ISO is significantly less depressant that HAL when muscle performance is compared at high stimulation rates. A previous study[1] reported that HAL does not demonstrate frequency-dependence, but our results concur with other studies[2] showing HAL has some degree of frequency-dependence. Since ISO's negative inotropic effects are more completely attenuated by stimulus conditions that increase trans-sarcolemmal $Ca^{2+}$ influx, it suggests that ISO's myocardial depressant action is more directly mediated by inhibition of trans-sarcolemmal $Ca^{2+}$ influx than HAL.

References

1. Lynch C: Differential depression of myocardial contractility by halothane and isoflurane in-vitro. Anesth. 64:620-631, 1986.

2. Komai H, Rusy BF: Negative inotropic effects of isoflurane and halothane in rabbit papillary muscles. Anesth. Analg. 66:29-33, 1987.

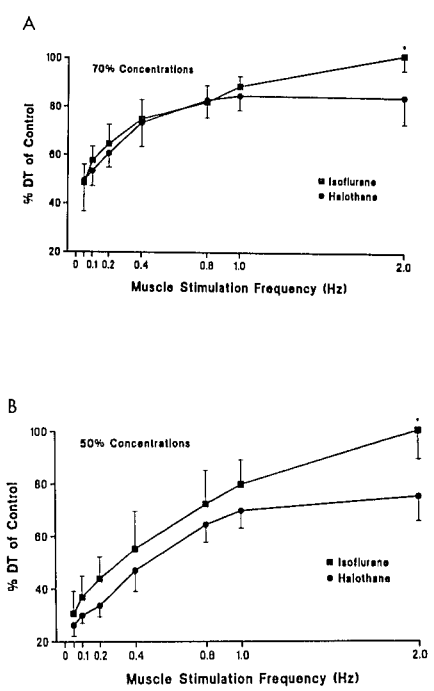


Figure 1. Alterations in DT (% of control) at similar cardiodepressant anesthetic concentrations of HAL and ISO at varying stimulus frequencies. A. Frequency-dependent depression of DT at the low (70% of control) anesthetic conc (halothane 0.8%; isoflurane 1.25%). B. Frequency-dependent depression of DT at the high (50% of control) anesthetic conc (halothane 1.35%; isoflurane 2.0%). Significant differences between anesthetics are indicated by the * (p=.001 at low conc; p<.0001 at high conc).