Title: ANESTHETIC UPTAKE AND ELIMINATION VIA BUBBLE OXYGENATORS: INFLUENCE OF ANESTHETIC, AND GAS AND PUMP FLOW RATES

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Introduction. Volatile anesthetic agents are often added to the gas mixture directed through the oxygenator during cardiopulmonary bypass (CPB), yet their uptake and elimination have not been studied. We measured anesthetic uptake and elimination by the blood perfusate of bubble oxygenators to address the following questions: 1) Does the rapidity of uptake and elimination differ among the anesthetics (isoflurane [I], enflurane [E], or halothane [H]), as a function of their blood/gas partition coefficients, in this setting? 2) What is the effect of altering the rate of gas inflow (oxygen) to the oxygenator? 3) What is the effect of altering the pump flow rate?

Methods. CPB circuits, each consisting of a roller pump and Bentley bubble oxygenator, were assembled. Whole blood diluted with crystalloid was added to produce a total priming volume of 2350 - 2550 ml with hemoglobin concentration of 8.5 - 10.3 gm/dL. The prime was recirculated through the oxygenator, filters, and tubing, without attachment to a patient. Temperature was maintained at 25 ± 1.5 °C and pH at approximately 7.4.

To examine the influence of anesthetic, we measured the concurrent rise of I, E, and H in the blood perfusate by administering a mixture 0.3 MAC of each agent during 5 experiments. Simultaneous samples of inlet gas and blood were obtained before the addition of anesthetic, at 1, 4, 8, 16, and 32 minutes during addition of anesthetic, and at the same intervals after discontinuation of anesthetic. In these experiments, gas inflow (a mixture of oxygen and sufficient carbon dioxide to maintain $P_aCO_2 \approx 40$ mm Hg) and pump flow rates were constant and equally matched at 3 l/min.

During studies examining the effect of gas flow variations (n=6), gas inflow was set at 3, 6, or 12 l/min, while pump flow remained stable at 3 l/min. During studies examining the effect of pump flow variations (n=5), pump output was set at 3 or 5 l/min, while gas inflow remained stable at 3 l/min. In each experiment, the sampling sequence was repeated either for each of the 3 gas flow rates or for the 2 pump flow rates. Only I was used for pump and gas flow comparisons.

Anesthetic concentrations in all samples were determined by gas chromatography and converted to partial pressures using the blood/gas partition coefficients determined in each study. (The mean blood/gas partition coefficients in this model of hemodilution and hypothermia were 1.16 ± 0.15 for I, 1.75 ± 0.21 for E, and 2.38 ± 0.28 for H.) Repeated measures analysis of variance was used to determine whether anesthetic choice or variations in the rate of gas inflow had a significant ($P < 0.05$) effect on rapidity of anesthetic uptake and elimination. Pump flow data were compared using paired T - tests.

Results. Figure 1 displays the rise of I, E, and H partial pressures in the blood (P_{BL}) toward inlet gas partial pressures (P_I) during uptake. The rate of rise of both I and E were significantly faster than that of H during the first 4 min; only E was significantly higher at 16 min. By 32 min, there were no differences among the three anesthetics. Figure 2 displays the decline in P_{BL} from the baseline blood partial pressures obtained just before cessation of anesthetic administration (P_{BLO}) during elimination. The rate of decline of I was significantly faster than that of H during the first 8 min; by 16 min, the effect was not significant. The rate of decline of E was intermediate and not significantly different from I or H.

Increasing gas inflow from 3 to 12 l/min resulted in a significantly faster increase in P_{BL}/P_I for I during the first 4 min of uptake (samples were not obtained at 8 min); by 16 min, the effect was no longer significant. Also, increasing gas inflow from 3 to 6 or 12 l/min resulted in significantly faster decline in P_{BL}/P_{BLO} during the first 16 min of elimination; the effect was no longer significant by 32 min. There were no differences in the anesthetic rate of rise (P_{BL}/P_I) or decline (P_{BL}/P_{BLO}) when pump flow rate was increased from 3 l/min to 5 l/min.

Discussion. Similarities among I, E, and H in the time courses of their uptake and elimination were more striking than any statistical differences in this *in vitro* model. Our data do suggest that uptake of both I and E administered via bubble oxygenators, and elimination of I, are more rapid than for H, as expected by the lower blood solubility of I and E. (The measured uptake of E is anomalous in that it rises faster than I.) This study also suggests that the desired anesthetic effect might be achieved even more rapidly if gas inflow is increased, particularly during the first few min of CPB. Similarly, when anesthetic administration is discontinued prior to termination of CPB, a rapid decline in anesthetic blood levels might be facilitated if I is used or if gas inflow is increased. These effects are similar to those obtained during inhalation administration of volatile anesthetic agents. Increasing pump flow had no significant effect, possibly because the increase was limited by the capabilities of the pump. Extrapolation of these findings to clinical situations should be done with caution, since the influence of tissue uptake was not present, nor was the influence of rewarming during anesthetic elimination. Studies in patients undergoing CPB are necessary to define these influences.

Figure 1: Anesthetic Uptake

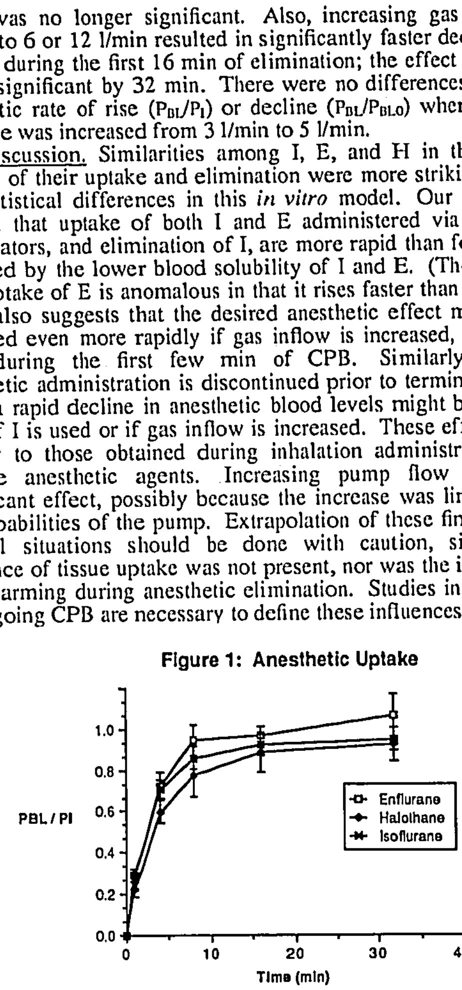

Figure 2: Anesthetic Elimination