Title: CARDIOVASCULAR EFFECTS OF THE VOLATILE ANESTHETICS DURING HYPOVOLEMIA

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Introduction. Although hypovolemia is usually corrected before the induction of anesthesia, the urgency of surgery may not permit this. The presence of hemodynamic instability then necessitates the use of a lower than usual dose of anesthetic. Since hemorrhage leads to stimulation of baroreceptors, sympathetic, and renin-angiotensin systems, an anesthetic which has minimal effects on these compensatory mechanisms could be the least deleterious. In the presence of normovolemia, halothane, enflurane, and isoflurane have distinct, dose dependent, cardiovascular effects which might influence their relative merit in the presence of hypovolemia. For example, systemic vascular resistance tends to be maintained with halothane; cardiac output tends to be maintained with isoflurane. This study was designed to determine whether the distinct effects of each agent seen during normovolemia persist when the agent is given at a low dose during hypovolemia.

Methods. 30 domestic swine (20.2±0.4kg) were briefly anesthetized (volatile anesthetic in N_2 and O_2) to allow the insertion of peripheral venous and systemic and pulmonary arterial cannulae. Each pig was intubated, paralyzed with metocurine, and mechanically ventilated to maintain P_aCO_2 at 40 mmHg. P_aO_2 was maintained at 150 to 210 mmHg. Administration of the anesthetic was then discontinued and each pig was studied awake, supine, and normovolemic 30 min. after the end-tidal anesthetic concentration had decreased to less than 0.05 MAC. Measurements were repeated after a blood volume reduction of 30% over 30 min. Each pig was then assigned randomly to 1 of 4 groups for anesthetic induction while hypovolemic: halothane, enflurane, isoflurane, or no agent (control). Measurements were made at 5 and 30 min. after the end-tidal anesthetic concentration became stable at 0.5% halothane, 1.25% enflurane, or 0.85% isoflurane (~0.5 MAC); control animals were studied at a comparable time. Shed blood was then returned, the anesthetic was discontinued, and measurements were made 30 min. after the anesthetic had decreased to less than 0.05 MAC. For each experimental condition, results among groups were compared using analysis of variance with repeated measures and Newman-Keuls' method of multiple comparisons. Statistical significance was accepted when $p<0.05$.

Results. There were no differences among the four groups in the normovolemic or in the awake, hypovolemic condition. 30% blood loss caused the expected cardiovascular, metabolic, and endocrine effects (Table 1). Halothane, enflurane, and isoflurane did not cause differing cardiovascular effects when used at a low dose to induce anesthesia during hypovolemia; all were different from control animals (Table 1). Each caused a decrease in systemic vascular resistance, cardiac output, and mean arterial blood pressure; plasma renin activity increased. Animals given enflurane had the highest blood lactate concentration. By 30 min. (anesthetic constant) blood pressure had recovered 48-60%, cardiac output had recovered 31-49%; systemic vascular resistance, heart rate, and cardiac filling pressure did not change significantly. When shed blood was returned and the anesthetic was discontinued there were no differences among the four groups. All animals survived.

Discussion. All three anesthetics interfered with the compensatory mechanisms for hemorrhage. In contrast to their effects when given in higher doses during normovolemia, they did not differ in their cardiovascular effects when given at a lower dose to induce anesthesia during hypovolemia. All agents decreased cardiac output and, despite an increase in plasma renin activity, decreased systemic vascular resistance. Enflurane caused the greatest imbalance in O_2 supply and demand as reflected by the highest lactate concentration. Despite a constant anesthetic dose, an improvement in myocardial performance over time was implied by an increase in cardiac output in the absence of a change in systemic vascular resistance, heart rate, cardiac filling pressure, or plasma catecholamine concentration. In conclusion, the cardiovascular effects of volatile anesthetics during normovolemia should probably not be extrapolated to the hypovolemic condition.

Table 1. Cardiovascular, metabolic, and endocrine effects of hemorrhage and induction of anesthesia during hypovolemia

Condition	BPa	Qt	SVR	HR	PCW	Lactate	PRA
Awake-Normovolemic	128	181	35	107	3	1.13	2.5
Awake-Hypovolemic[a]	97	111	44	155	0	1.86	9.1
5 min.							
No agent	97[b]	118[b]	42[b]	162[c]	1[c]	1.43[d]	6.8[e]
Halothane	36	67	26	145	2	1.97	23.1
Enflurane	28	65	21	150	0	3.62	17.2
Isoflurane	29	61	25	121	1	2.48	25.5
30 min.							
No agent	108[b]	124[b]	45[b]	164[c]	1[c]	1.42[d]	8.1
Halothane	55	88	30	130	2	2.04	29.5[f]
Enflurane	43	86	24	152	1	3.25	16.1
Isoflurane	43	91	26	137	2	2.48	18.4

Data are means for 7, no agent; 7, halothane; 8, enflurane; 8, isoflurane animals.
BPa, mean systemic blood pressure (mmHg); Qt, cardiac output (ml/kg/min); SVR, systemic vascular resistance (mmHg/l/min); HR, heart rate (bpm); PCW, pulmonary capillary wedge pressure (mmHg); Blood lactate (mmole/l); PRA, plasma renin activity (ng/ml/min).
Statistical analysis:
[a] all variables significantly different from normovolemic values
[b] control > all anesthetics
[c] no difference among groups
[d] enflurane > control, halothane, isoflurane; isoflurane > control
[e] control < all anesthetics
[f] halothane > control, enflurane, isoflurane