TITLE: CHRONIC HYPOKALEMIA ON EPINEPHRINE-INDUCED DYSRHYTHMIAS DURING HALOTHANE, ENFLURANE OR METHOXYFLURANE WITH N_2O ANESTHESIA

AUTHORS: K. C. Wong, M.D., Ph.D., C. K. Tseng, M.D., B. A. Puerto, M.D. and A. X. Puerto, M.D.

AFFILIATION: Department of Anesthesiology, University of Utah College of Medicine, Salt Lake City, Utah 84132

Chronic hypokalemia is known to increase cardiac excitability during acid-base disturbance, especially alkalosis from hyperventilation. Significant reduction of intracellular potassium, alters the relationship between the resting membrane potential and the threshold of excitation of cardiac cells, should also potentiate catecholamine-induced dysrhythmias. We have recently shown in dogs that halothane, enflurane or methoxyflurane administered with N_2O lowered the arrhythmogenic doses of epinephrine in these halogenated agents when compared with data where these anesthetics were administered with O_2 without N_2O.[1] The purpose of this study was to determine the influence of hypokalemia from chronic furosemide treatment on epinephrine-induced dysrhythmias during halothane, enflurane or methoxyflurane with N_2O anesthesia in dogs.

METHOD: Ten mongrel dogs weighing 15-20 kg were mechanically ventilated to maintain a $PaCO_2$ of 35-40 torr. Each animal received 1.2 MAC halothane (1.0%), enflurane (2.6%) or methoxyflurane (0.28%) in 50% N_2O and 50% O_2 and the end tidal CO_2 and the halogenated anesthetic concentrations were continuously measured by Beckman Infra Analyzers. Each animal was studied 3 times but only one anesthetic regimen per study on a given day. The order of administration of the anesthetic regimen was randomized.

Continuous monitor was made of lead II ECG, esophageal temperature and arterial pressure. The arterial pressure was taken from a catheter inserted in the femoral artery from which blood gas and serum [Na] and [K] were determined. Five percent dextrose in lactated Ringer's solution (8-18 ml/kg/hr) was infused to maintain a mean arterial pressure of 80 ± 10 torr prior to each epinephrine infusion. Epinephrine was infused at 1 ug/kg/min up to 10 minutes with a Harvard syringe pump. The appearance of ventricular tachycardia or ventricular fibrillation was cause to discontinue the epinephrine infusion before the completion of 10 ug/kg/10 min total dose. The persistence of 3 or more consecutive dysrhythmic beats was used as the end-point of the epinephrine arrhythmogenic dose. Twenty-one out of 30 epinephrine infusions received the total calculated dose of 10 ug/kg/10 min.

Chronic hypokalemia was induced by administration of furosemide (2 mg/kg IV) for at least 14 days. Serum electrolytes were measured at 3 day intervals during daily furosemide. Paired t-test was used to compare data; $p<.05$ was considered significant.

RESULTS: No significant differences were observed in arterial pCO_2, pH and serum [Na], between pretreatment and furosemide treated dogs, but serum [K] was reduced by about 30% following the diuretic treatment (Table 1). These measurements did not change appreciably during epinephrine infusion. MAP before and peak MAP after epinephrine infusion were not significantly different among the 3 anesthetic groups (Table 2). The arrhythmogenic doses of epinephrine for the appearance of ventricular dysrhythmia were also not different among the groups, but the incidence of PVC's was less for methoxyflurane-N_2O anesthesia. Incidence of VT or VF was also higher for halothane and enflurane in comparison with methoxyflurane (Table 2).

DISCUSSION: The results of this study are similar to the animals not treated with furosemide.[1] The only difference is that infusion of epinephrine in normokalemic dogs was associated with an increase in serum [K] from 4.1 to 6.5 mEq/L, whereas in the present experiment serum [K] only increased from 3.22 to 3.55 mEq/L. The difference may be that furosemide treated animals had less K^+ to be mobilized by epinephrine infusion. The incidence of VT or VF in the hypokalemic dogs of this study is also similar to normokalemic animals receiving the same anesthetic regimen.[1] If these hypokalemic animals were hyperventilated, presumably they may be more prone to develop serious catecholamine-induced dysrhythmias. These results suggest that hypokalemic animals may have a higher incidence of epinephrine-induced VT or VF during halothane-N_2O in comparison with enflurane-N_2O anesthesia, whereas methoxyflurane-N_2O anesthesia was not associated with the development of these serious dysrhythmias.

References.

1. Puerto BA, Wong KC, Puerto AX, et al: Epinephrine-induced dysrhythmias: Comparison during anesthesia with narcotics and with halogenated inhalation agents in dogs. Canad Anaesth Soc J, July, 1979 (In Press)

TABLE 1. Effects of Furosemide Treatment on Serum [K] and [Na] and Arterial PCO_2 and pH During Maximal MAP

	Pretreatment	Furosemide Treated	After Epinephrine
Serum [Na] (mEq/L)	146.2 ±4.1	144.5 ±4.7	142.2 ±5.2
Serum [K] (mEq/L)	4.6 ± .27	3.22± .18*	3.55± .27+
PCO_2 (torr)	35.3 ±2.2	34.7 ±1.6	40.7 ±4.5
pH	7.36±0.05	7.36±0.04	7.28±0.06

*$p < .05$, Paired t-test compared with pretreatment values (N=10)

+$p < .05$, Compared with furosemide treated (N=10)

TABLE 2. Effects of Epinephrine-Infusion (1 ug/kg/min) on Arterial Blood Pressure and Cardiac Dysrhythmias During Halogenated Anesthesia (1.2 MAC) and N_2O (50%)

	Control MAP (torr)	Peak MAP aft. Epi. (torr)	PVC, Epi. Dose (ug/kg)	VT or VF
Halothane	78±15	165±40	2.78±1.2(10/10)	5.1±1.7(6/10)
Enflurane	75±22	160±32	3.65±1.1(10/10)	4.4±1.6(3/10)
Methoxyfl.	82±25	174±46	3.20±0.9(6/10)	--- (0/10)

Numbers in parenthesis indicate incidence of cardiac dysrhythmia (N=10); MAP = mean arterial pressure; PVC = premature ventricular contractions; VT = ventricular tachycardia; VF = ventricular fibrillation