

Title: Hemodynamic Effects of Anesthetic Doses of Alpha-Prodine and Sufentanil in Dogs
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Large doses of morphine (2-3 mg/kg) or fentanyl (50-100 ug/kg) produce complete anesthesia and little circulatory changes in dogs and man during oxygen breathing. Although anesthetic doses of fentanyl result in less detrimental side effects than comparable doses of morphine, both techniques cause post-operative respiratory depression and other annoying problems. A narcotic compound that is capable of producing complete anesthesia, results in little or no alteration in circulatory dynamics and is possessed of less side effects than either morphine or fentanyl, would be an improvement as a narcotic anesthetic. Recent work in our laboratories has demonstrated that alpha-prodine (nisentil) and sufentanil (a new synthetic narcotic not yet available in this country) are capable of producing complete anesthesia when administered intravenously in sufficient quantities. This study was designed to investigate the cardiovascular effects of equi-anesthetic doses of each of these compounds in the dog.

Thirty mongrel dogs (15-25 kg) served as the experimental subjects. Each had a large bore intravenous catheter placed in a foreleg vein, was induced with 20-25 mg/kg of sodium thiopental and had its trachea intubated. Respirations were controlled with pure oxygen at a rate sufficient to keep PaCO₂ between 32-36 torr. A quadruple lumen Swans-Ganz catheter was placed in the pulmonary artery via the right internal jugular vein for determination of cardiac output (Q_T) via the thermodilution technique and measurement of mean pulmonary artery (PAP), mean pulmonary capillary wedge (PCWP) and mean right atrial pressures (RAP).

A second catheter was inserted into the aorta through the femoral artery and used for blood gas sampling and measurement of mean arterial blood pressure (BP). Fifteen dogs (8 in group IA and 7 in group IB) received alpha-prodine and 16 dogs (8 each in groups IIA and IIB) received sufentanil. Dogs in the A groups received atropine (1.5 mg, intramuscularly) 15-20 minutes before anesthetic induction. Dogs in the B groups received no premedication. Fifteen minutes after completion of instrumentation, dogs in groups IA and IB were given alpha-prodine at a rate of 0.1 mg/kg/min and dogs in groups IIA and IIB received sufentanil at a rate of 10 ug/kg/min. After one hour, infusion of alpha-prodine was increased to 0.2 ug/kg/min in groups IA and IB and continued for an additional 70 minutes. In groups IIA and IIB infusion of sufentanil was increased to 20 ug/kg/min after 30 minutes and 40 ug/kg/min after 60 minutes and continued at this rate for an additional 70 minutes. Heart rate (HR), BP, Q_T, PAP, PCWP, RAP and pulmonary (PVR) and systemic vascular resistances (SVR) were measured before narcotic administration and 30, 60 and 90 minutes later. After the 90 minute measurement all dogs were given 60% nitrous oxide in oxygen to breathe and 15 minutes later 60% N₂O in oxygen. Fifteen minutes after breathing this latter mixture naloxone (0.4 mg) was given intravenously. Cardiovascular dynamics

were recorded 15 minutes after breathing N₂O and N₂ and 5 and 10 minutes after naloxone.

Dogs in the A groups had significantly higher control (pre-narcotic infusion) HR and Q_T and lower SVR than dogs in the B groups, however, all other variables were similar in the two groups, Table 1. Dogs in group IIA experienced a slight decrease in HR after 30 minutes of sufentanil but no significant change in any other variable. No variable was changed in this group during the remainder of the study except PVR and SVR which were increased following addition of N₂O and again after naloxone. Group IIB dogs sustained significant decreases in HR, BP and Q_T after 30 minutes but experienced no significant further changes in these or any other variables throughout the remainder of the study with the exception of SVR which was increased following N₂O and again after naloxone. Naloxone did not reverse the anesthetic state in any dog in group IIA or IIB. Infusion of alpha-prodine decreased HR, BP, Q_T, and SVR and increased PVR after 30 minutes but did not change PAP, PCWP, or RAP in groups IA and IB. Continued infusion of alpha-prodine at 0.1 mg/kg/min or increasing infusion of 0.2 mg/kg/min did not further influence any of these variables. Changing the inspired mixture of gases to 60% N₂O in O₂ increased BP, PAP, PVR and SVR and reduced Q_T but did not further change any other variable in groups IA and IB. Inspiration of 60% N₂ instead of N₂O returned all variables to pre-N₂O values. Administration of naloxone in groups IA and IB produced similar changes as did inspiration of N₂O with the exception that Q_T was not changed. Naloxone reversed the anesthetic effects of all dogs anesthetized with alpha-prodine.

The results of this study demonstrate that anesthetic doses of sufentanil produce little change in cardiovascular dynamics in atropinized dogs and only small decreases in HR, BP and Q_T in dogs without atropine premedication irrespective of the infusion rate. In contrast, alpha-prodine results in significant cardiovascular depression irrespective of the presence or absence of atropine pre-medication. In addition, N₂O and naloxone produce further cardiovascular depression while increasing BP in alpha-prodine anesthetized dogs but only mildly increase PVR and SVR in sufentanil anesthetized animals. Our data suggest that large doses of sufentanil deserve evaluation as a narcotic anesthetic in man.

TABLE 1

	Control	Mins of Infusion			60% N ₂ O +	60% N ₂	Minutes after Naloxone		
		30	60	90	O ₂	O ₂	5	10	
HR (bts/min)	IA	148	115#	107#	106#	104#	106#	103#	108#
	IB	110	99*	98*	95*	94*	95*	94*	96*
	IIA	136	112#	104#	98#	99#	95#	92#	99#
	IIB	114	89#	86#	78#	82#	84#	85#	88#
BP (torr)	IA	131	111#	111#	116#	129	120*	179#	172#
	IB	130	93#	92#	98#	118	100#	147*	154#
	IIA	128	122	124	124	130	128	134	132
	IIB	126	112*	111*	116*	111*	112*	114*	113*
Q _T (l/min)	IA	2.9	2.4*	2.4*	2.2*	1.7#	2.3*	2.1*	2.1*
	IB	2.0	1.5*	1.4*	1.4*	1.2#	1.6*	1.5*	1.5*
	IIA	2.6	2.6	2.5	2.4	2.2	2.5	2.2	2.3
	IIB	2.0	1.7*	1.6*	1.7*	1.6*	1.6*	1.6*	1.6*

*P < .05, #P < .01, Student's paired t-test when compared to control values.