TITLE: CARDIAC OUTPUT AND ITS DISTRIBUTION IN DOGS HEMODILUTED WITH 5% ALBUMIN OR 10% HEMOGLOBIN

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Introduction. Hemodilution is usually the result of intentional replacement of red cell mass with crystalloid or colloid solution.[1] Synthetic colloids that carry oxygen (hemoglobin-based) may soon be added to the regimen of transfusion and resuscitation fluids. However, unlike classic hemodilution with saline or albumin, hemoglobin does not augment cardiac output.[2] Hemoglobin colloid may affect peripheral blood flow and the distribution of cardiac output such that venous return is not augmented. The present study tests this hypothesis.

Methods. Seven dogs anesthetized (Na pentobarbital) and mechanically ventilated with 100% O_2. Mean aortic-MAP and central venous-CVP pressures, heart rate-HR, organ blood flows (microsphere) measured. Fractional distribution of cardiac output (CO) computed from (BF)÷(CO), where BF (ml/min) = organ flow (ml/min/100g) x organ weight(g) and CO is sum of organ flows. Muscle, skin and bone weights calculated as 40%, 9% and 8% of body weight respectively. Colloid osmotic pressure (COP; mmHg) was 19.3 ± 0.6 for 5% Ab and 29.8 ± 0.9 for 10% Hb. Hemodilution via isovolemic exchange of blood for colloid (≈45ml/kg). Significance from pre-colloid baseline with paired t-test.

Results.

Systemic Hemodynamics Pre and Post Hemodilution

	pre-Ab	post-Ab	pre-Hb	post-Hb
CO (L/min)	2.32 ± 0.16	3.77 ± 0.20(↑)	1.56 ± 0.23	1.86 ± 0.45
AOP (mmHg)	118 ± 4	111 ± 6	115 ± 10	122 ± 7
HR (b/min)	179 ± 9	180 ± 9	150 ± 6	145 ± 6
CVP (mmHg)	5.3 ± 0.3	5.0 ± 0.7	4.8 ± 0.5	5.1 ± 0.6
COP (mmHg)	17.6 ± 0.7	19.1 ± 0.8	18.4 ± 0.3	23.8 ± 1.1(↑)
Hct (vol%)	45 ± 2	23 ± 1(↓)	45 ± 3	22 ± 2(↓)

Fractional Distribution of Cardiac Output

	pre-Ab	post-Ab	pre-Hb	post-Hb
kidney	38.3 ± 1.1	22.7 ± 3.7(↓)	37.5 ± 1.8	21.6 ± 3.4(↓)
GI tract	12.8 ± 1.4	17.4 ± 1.5(↑)	9.5 ± 0.9	15.7 ± 1.5(↑)
pancreas	0.6 ± 0.1	0.6 ± 0.1	0.6 ± 0.2	0.7 ± 0.1
spleen	8.8 ± 1.1	7.8 ± 0.5	8.0 ± 1.3	3.5 ± 0.8(↓)
omentum	0.6 ± 0.2	0.8 ± 0.2	0.4 ± 0.1	0.7 ± 0.1(↑)
liver	7.2 ± 2.8	8.5 ± 1.3	7.6 ± 1.1	12.5 ± 0.7(↑)
lung	2.7 ± 0.5	2.1 ± 0.5	2.8 ± 0.6	1.2 ± 0.4(↓)
muscle	11.8 ± 2.4	16.1 ± 1.3	12.5 ± 0.7	22.0 ± 1.6(↑)
skin	2.1 ± 0.4	4.2 ± 0.9	3.0 ± 0.4	2.7 ± 0.3
bone	8.4 ± 1.7	8.1 ± 0.5	12.9 ± 1.3	7.2 ± 1.7(↓)
left vent.	3.2 ± 0.6	4.2 ± 0.9(↑)	3.2 ± 0.6	6.9 ± 0.6(↑)
right vent.	1.4 ± 0.3	2.7 ± 0.6(↑)	0.7 ± 0.1	1.8 ± 0.1(↑)
Brain	2.1 ± 0.8	2.8 ± 1.1	1.3 ± 0.1	3.5 ± 0.6(↑)

Values = mean ± SE, n=7. ↑, ↓ P<0.05 from respective baseline.

Conclusion. AOP, HR, CVP, Hct and COP suggest constant total blood volume in Hb dogs. Hemodilution with Hb colloid does not result in augmented CO or venous return because CO is preferentially distributed to capacitance beds (GI tract, liver, muscle) where venous pooling may be occurring (conversion of stressed volume to unstressed volume).[3]

References
1. Messmer K, et al, Prog Surg 13:208,1974.
2. Rosen L, et al, Crit Care Med 7:380, 1979.
3. Rothe C, Handbook Physiol 3:397, 1983.

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TITLE: MIDAZOLAM AND FLUMAZENIL DECREASE VASCULAR TONE IN THE ISOLATED DOG SAPHENOUS VEIN PREPARATION

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INTRODUCTION: Benzodiazepines are known to decrease peripheral sympathetic tone by an action on gabamingeric neurons in the central nervous system. Cardiovascular studies in dog suggest the blood pressure decrease following I.V. midazolam (MID) may involve binding to peripheral vascular benzodiazepine receptors. Experiments therefore were conducted using an isolated saphenous vein preparation to determine MID and the antagonist Flumazenil's action on vascular smooth muscle tone.

METHODS: Twenty-eight helical strips weighing 50-80mg were carefully prepared from dog saphenous vein segments. Each segment was mounted between platinum field stimulation electrodes in a 5ml isolation tissue bath containing Kreb Bicarbonate buffer pH 7.4 with cocaine and corticosterone added to block the uptake of norepinephrine (NE) released by the field stimulation. The bath was maintained at 37°c and aerated with 95% O_2-5% CO_2. The vein segment was attached to a calibrated Harvard isotonic force displacement transducer and the change in vascular tension recorded on a X-Y recorder. The tissue was subjected to a 2.0 gram preload tension. Electrical field stimulation was applied across the tissue at 2Hz, 5.0 msec duration and supermaximal voltage.

RESULTS: Vascular tension in grams/100mg tissue weight increased an average of 7.8±0.97 SEM due to field stimulation. A further increase in tension to 10.38±1.15 ($p<.05$) occurred after adding the NE uptake blockers. A significant $p<.05$ decrease in vascular tension occurred with the addition of MID 10^{-4} and 10^{-3}M, 10.54±1.08 to 6.01±0.94 and 10.93±1.15 to 1.64±0.32 gm/100mg respectively. The addition of 0.05-0.10 mg/ml Flumazenil (10^{-4}M) did not reverse MID 10^{-4}M, but caused a further decrease in vascular tension similar to MID 10^{-4}M. The decreased tension due to MID 10^{-4}M and Flumazenil was reversed by repeated CG Kreb Buffer flushing and by the addition of NE $1x10^{-5}$M or epinephrine $1x10^{-5}$M. The addition of tolazoline 10^{-3}M caused a decrease in vascular tension similar to that observed from 10^{-3}M MID.

DISCUSSION: The results obtained demonstrate an action of MID to decrease vascular tone that is not mediated via a benzodiazepine action in the central nervous system. Further, the vasodilatory action is dose dependent. Ebert et al reported a decrease in measured sympathetic nerve activity following MID which the authors concluded was the mechanism of the blood pressure decrease by MID. Results from this isolated vein study suggest however, that the primary mechanism for the observed blood pressure decrease is a direct action of MID or peripheral vessels. Further, the decrease in vascular tension observed with Flumazenil suggest a common action with MID on vascular tone that differs from their agonist/antagonist actions in the central nervous system. Anesthesiology 71, 1989