TITLE: EFFECTS OF CLONIDINE PREMEDICATION IN NEUROSURGICAL PATIENTS

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The effectiveness of clonidine premedication in blunting the hemodynamic and endocrine response to surgery (1) was examined in patients scheduled for elective craniotomies (with informed consent and approval by the local hospital research committee).Two groups of patients were examined in a double blind fashion: Group C (n=9) received clonidine (300 µg p.o.) 90 min prior to baseline (BL) evaluation, Group P (n=10) received p.o. placebo.Anesthesia was induced with thiopental (5mg/kg I.V.), isoflurane,vecuronium bromide (0.1 mg/kg I.V.),and was maintained with N2O/isoflurane. Mean arterial blood pressure (MABP,radial artery catheter) and heart rate (HR) were continuously monitored.Arterial blood samples for the measurement of plasma norepinephrine (NE),epinephrine (EPI), cortisol, aldosterone,and glucose were collected at BL=prior to induction of anesthesia,2 min after intubation,at the beginning of surgery,and 2 min after extubation.

Both groups were comparable with regard to age, body weight, ASA-status (I-II), duration of intervention (ca.3 hr),and fluid administration (ca.450 ml/hr).Patients pretreated with clonidine required less isoflurane (0.5 vol %) as compared to control (0.66 vol %).The clonidine group showed lower HR,MABP,cortisol and aldosterone levels throughout the study,and blood glucose levels at extubation,as compared to control. (Table 1).Though,the mean catecholamine plasma leves were not different between the groups,clonidine treatment led to a significant decrease in intra-patient variablility of NE levels (CV:25 %) as compared to control (CV:45 %).

These data confirm the anesthesia sparing,and hemodynamic suppressant effect of clonidine (1),and newly show a significant suppression of the adrenal cortical response to surgery,which is probably due to alpha2 receptor mediated ACTH suppression (2).The lower increase in blood glucose levels,obserevd with clonidine,at the end of surgery may be beneficial in neurosurgical patients.

References:1) Anesthesiology,67:11-19,1987
2) J.Cardiovasc.Pharmacol.10 (Suppl.12):S235-39,1987

Table 1: Summary of Results

	Group	BL	Intubation	Surgery	Extubation
MABP (mm Hg)	P	95.5 (±5.0)	118† (±8.3)	92.8 (±6.0)	112 (±4.9)
	C	85.3* (±4.1)	101†* (±8.2)	86.7* (±8.6)	102* (±7.8)
HR (bpm)	P	77.0 (±4.1)	90.1† (±4.9)	77.5 (±3.4)	94.3 (±5.3)
	C	61.1* (±3.7)	78.7†* (±6.5)	69.3* (±7.7)	76.3* (±5.2)
EPI (nmol/L)	P	0.39 (±0.09)	0.37 (±0.10)	0.36 (±0.07)	0.46 (±0.08)
	C	0.36 (±0.14)	0.22 (±0.07)	0.32 (±0.13)	0.41 (±0.17)
NE (nmol/L)	P	2.10 (±0.54)	2.78 (±0.67)	2.46 (±0.85)	2.81 (±0.50)
	C	2.34 (±1.10)	2.12 (±0.89)	2.19 (±0.81)	2.01 (+0.97)
Glucose (mmol/L)	P	5.76 (±0.44)	5.83 (±0.44)	6.37 (±0.24)	8.29† (±0.40)
	C	6.13 (±0.20)	5.93 (±0.23)	6.98 (±0.24)	6.71†* (±0.28)
Cortisol (nmol/L)	P	749 (±149)	772 (±151)	711 (±128)	981 (±81.3)
	C	352* (±128)	267* (±78.8)	170†* (±35.6)	525* (±142)
Aldosterone (nmol/L)	P	0.38 (±0.07)	0.31 (±0.06)	0.42 (±0.07)	0.83† (±0.13)
	C	0.24* (±0.08)	0.19* (±0.04)	0.19* (±0.05)	0.39†* (±0.09)

Values expressed as mean ±SE.* p<0.05 between group comparison, † p<0.05 within group comparison to BL.

TITLE: THE RESPONSE OF THE CANINE CEREBRAL CIRCULATION TO HYPERVENTILATION DURING ANESTHESIA WITH DESFLURANE

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Introduction

Arterial CO_2 tension ($PaCO_2$) is an important factor in controlling cerebral vascular resistance (CVR) and cerebral blood flow (CBF) in healthy animals and man. The potent vasoconstrictor effect of hypocarbia has been shown to predominate over the vasodilating effects of both halothane and isoflurane. The present study was designed to examine the effects of normocarbia and 2 levels of hypocarbia on CBF, CVR, and ICP at clinically relevant concentrations of desflurane in dogs.

Methods

Following approval by the animal care and use committee, cerebral studies were done in 5 dogs. Anesthesia was induced with halothane and oxygen in an airtight chamber. The animals were paralyzed with pancuronium, intubated, and mechanically ventilated with desflurane (1.5 MAC - 10.5%) O_2, N_2. Cannulae were inserted into a femoral artery for blood sampling and pressure measurement, into a femoral vein for blood return from the CBF measurement, and into the sagittal sinus for direct measurement of CBF and cerebral metabolic rate for oxygen ($CMRO_2$). A fiberoptic intracranial monitoring device and a thermistor probe were inserted into the parietal epidural space. Three levels of $PaCO_2$ were studied in random order at each MAC concentration (0.5, 1.0, 1.5) of desflurane. Each study period consisted of measurements of HR, MAP, CBF, $CMRO_2$, ICP, EEG, ABG, blood glucose and lactate.

Results

CBF decreased significantly with hyperventilation to PCO_2 = 20 mmHg at each concentration studied, while CVR increased significantly (Table 1). ICP did not change significantly with hyperventilation.

The Effects of Desflurane and Hyperventilation on Cerebral Hemodynamics and Metabolism

MAC Desflurane	PCO_2 mmHg	CBF ml·min^{-1}·100g^{-1}	CVRI mmHg·ml·min^{-1}·100g^{-1}	ICP mmHg	$CMRO_2$ ml·min·100g	MAP mmHg
0.5	40 ± 1	81 ± 6	1.33 ± 0.20	13 ± 2	3.41 ± 0.32	127 ± 7
	32 ± 0*	54 ± 3*	1.94 ± 0.26*	9 ± 1	3.83 ± 0.30*	122 ± 6
	24 ± 1*†	40 ± 3††	2.47 ± 0.40*†	10 ± 1	4.00 ± 0.34	113 ± 7*†
1.0	40 ± 1	79 ± 10	0.63 ± 0.03	14 ± 3	3.13 ± 0.30	74 ± 4
	31 ± 1*†	70 ± 6	0.75 ± 0.07	17 ± 3	3.45 ± 0.30	78 ± 6
	22 ± 1††	43 ± 5	1.59 ± 0.35	11 ± 2	3.56 ± 0.30*	83 ± 9
1.5	40 ± 0	65 ± 6	0.60 ± 0.06	15 ± 3	2.56 ± 0.20	63 ± 3
	31 ± 1	45 ± 2	0.82 ± 0.09	13 ± 1	2.42 ± 0.40	60 ± 4
	23 ± 1	38 ± 2	1.05 ± 0.25	11 ± 1	2.48 ± 0.60	60 ± 9

Values are ± SEM
*Significantly different from pCO_2 = 40 ($p < 0.05$)
†Significantly different from pCO_2 = 30 ($p < 0.05$)

Discussion

The results of this study indicate the cerebral vasculature remains responsive to changes in pCO_2 at all concentrations studied, and are similar to those of isoflurane. The ICP did not change significantly with hyperventilation despite the changes in CBF and CVR. It is hypothesized that desflurane even at 0.5 MAC significantly increases CBV to account for the observed increase in ICP. Because CBV is less responsive than CBF to hypocarbia, ICP did not change with hyperventilation.