Title: EFFECT OF ADRENERGIC DRUGS ON CEREBRAL BLOOD FLOW, METABOLISM AND EVOKED POTENTIALS AFTER DELAYED ONSET OF CPR IN DOGS.

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INTRODUCTION: We previously showed that equipotent pressor doses of phenylephrine (PHE) and epienephrine (EPI) administered immediately after the onset of cardiac arrest during CPR were equally effective in maintaining cerebral blood flow (CBF), cerebral O_2 uptake ($CMRO_2$), and brain conductive function, as assessed by somatosensory evoked potentials (SEP) in adult dogs (1). Others have found that PHE is less effective when the onset of CPR is delayed in pigs (2). We currently compared the efficacy of EPI and PHE when the onset of CPR is delayed 8 min after arrest. We also determined whether EPI by its β-agonist properties increases $CMRO_2$ more than PHE and if so, if this is reflected in differences in recovery of SEP. In addition, we pretreated one group of dogs with a lipophilic β-adrenergic antagonist, pindolol, to test whether $CMRO_2$ would be lower with EPI treatment during CPR.

METHODS: Adult mongrel dogs (~22 kg) were anesthetized with iv fentanyl (50 μg/kg) and pentobarbital (6 mg/kg bolus plus 3-6 mg/kg/hr) and mechanically ventilated through a tracheostomy. Mean aortic (MAP) and lateral ventricle (ICP) pressures were measured. CBF was determined by the radiolabeled microsphere technique. $CMRO_2$ was calculated using arterial and sagittal sinus O_2 contents. SEP were generated by foreleg stimulation; amplitude (S-AMP) of primary cortical wave was measured. After induction of ventricular fibrillation, ventilation was discontinued. After 8 min of cardiac arrest, simultaneous compression and ventilation CPR commenced using a pneumatic chest compressor set to a rate of 40/min with a 50% duty cycle. Airway pressures were 100-120 cm H_2O. Immediately after commencing CPR, 7 animals (group EPI) received 1 mg EPI followed by a continuous iv infusion of 4 μg/kg/min; 5 animals (group PHE) received 1 mg PHE followed by an infusion of 20 μg/kg/min; 6 animals (group P+E) received pretreatment with pindolol, 2 mg/kg before induction of cardiac arrest, and during CPR the same epinephrine treatment as EPI group. After 6 min of CPR, defibrillation was attempted. If unsuccessful within 4 attempts, animals were excluded from the study. After defibrillation, EPI or PHE infusion was weaned within 10 min. Measurements continued for 240 min after resuscitation. Sodium bicarbonate was used to correct pH and lactated Ringer's solution was infused at 120 ml/hr. Data are presented as mean ± SE.

RESULTS: During CPR, MAP and ICP were similar in all groups. CBF of 42-60 ml/min/100g was generated during CPR (Table). Cerebral hypoperfusion occurred during the recovery period in all groups. During CPR, $CMRO_2$ was maintained in the EPI and PHE groups, and increased in the P+E group. During the recovery period, $CMRO_2$ diminished to below control values in the EPI and PHE groups. S-AMP remained flat during CPR and only partially recovered after resuscitation. There was no difference in S-AMP among groups.

DISCUSSION: CBF during CPR is maintained at similar levels regardless of the drug regimen used. The observation that $CMRO_2$ was not higher with EPI than with either PHE or P+E indicates that it is unlikely that high dose EPI administration causes cerebral hypermetabolism during CPR. Our data show that PHE, in an appropriately high dose, can be as effective as EPI in enhancing vital organ perfusion whether or not there is a significant delay in the onset of CPR. Moreover, we found no difference between EPI or PHE treatment on recovery of $CMRO_2$ or SEP. (Supported by NIH NS20020).

REFERENCES:

1. Schleien et al.: Anesthesiology 67:A650, 1987
2. Brown et al.: Resuscitation 14:171, 1986

		Pre-Arrest	CPR	Post-Resuscitation 10 min	30 min	120 min	240 min
MAP	EPI	111 ± 5	72 ± 4	87 ± 9	98 ± 9	114 ± 8	105 ± 11
mmHg	PHE	117 ± 9	71 ± 8	123 ± 8	117 ± 5	114 ± 3	105 ± 3
	P+E	119 ± 9	86 ± 2	96 ± 12	114 ± 16	96 ± 9	81 ± 8
CBF	EPI	31 ± 4	51 ± 16	30 ± 3	21 ± 3	15 ± 1	18 ± 2
ml/min/100g	PHE	40 ± 10	42 ± 15	61 ± 15	31 ± 10	20 ± 3	25 ± 4
	P+E	25 ± 2	60 ± 10	39 ± 3	23 ± 2	17 ± 1	22 ± 5
$CMRO_2$	EPI	2.7 ± 0.2	3.4 ± 0.8	1.6 ± 0.4	1.8 ± 0.3	1.7 ± 0.1	2.0 ± 0.1
ml/min/100g	PHE	3.1 ± 0.5	3.2 ± 1.1	1.4 ± 0.3	2.1 ± 0.1	1.8 ± 0.2	2.8 ± 0.6
	P+E	2.3 ± 0.3	5.2 ± 1.4	1.3 ± 0.4	2.1 ± 0.2	2.3 ± 0.2	2.3 ± 0.2
S-AMP	EPI	100 ± 0	0	57 ± 10	75 ± 21	70 ± 21	72 ± 23
% control	PHE	100 ± 0	0	35 ± 18	50 ± 17	66 ± 29	59 ± 12
	P+E	100 ± 0	0	36 ± 8	73 ± 13	71 ± 13	68 ± 17