TITLE: COMPARISON OF PHENYLEPHRINE AND EPINEPHRINE ON CEREBRAL AND MYOCARDIAL PERFUSION AND SOMATOSENSORY EVOKED POTENTIALS DURING AND FOLLOWING CARDIOPULMONARY RESUSCITATION IN DOGS

AUTHORS: C. L. Schleien, M.D., R. C. Koehler, Ph. D., I. D. Berkowitz, M.D., J. M. Dean, M.D., H. Gervais, M.D., J. R. Michael, M. D., M. C. Rogers, M.D., R. J. Traystman, Ph.D.

AFFILIATION: Department of Anesthesiology and Critical Care Medicine, Johns Hopkins Medical Institutions, Baltimore, MD 21205

Introduction: Epinephrine (EPI) improves cerebral (CBF) and myocardial (MBF) blood flow during cardiopulmonary resuscitation (CPR) by elevating perfusion pressure via peripheral vasoconstriction. We assessed if phenylephrine (PE) by its alpha-agonist properties also sustains high levels of CBF and MBF during CPR, and whether this leads to successful resuscitation. In addition, we determined whether EPI by virtue of its beta adrenergic properties, increases cerebral oxygen uptake more than PE, and if so, whether this is reflected in differences in somatosensory evoked potentials (SEP) during and following CPR.

Methods: Dogs (19-22 kg) were anesthetized with iv fentanyl (50 ug/kg) and pentobarbital (6 mg/kg bolus plus 3-6 mg/kg/hr) and mechanically ventilated through a tracheostomy. Mean vascular pressures (mm Hg) were measured in the intrathoracic aorta (MAP), and lateral ventricle (ICP). Cerebral perfusion pressure (CPP) was calculated as MAP minus ICP. CBF and MBF (ml/min/100g) were determined by the radiolabeled microsphere technique. Cerebral $O_2$ uptake ($CMRO_2$, ml $O_2$/min/100g) was calculated using $O_2$ content measured in arterial and sagittal sinus blood samples. The fraction of $O_2$ extracted by the cerebrum (EXT) was calculated from the arterial-sagittal sinus $O_2$ content difference divided by the arterial $O_2$ content. Simultaneous compression and ventilation CPR was performed at a rate of 40 compressions/min with a compression duty cycle of 50% and airway duty cycle of 40%. Airway pressures were 80-85 cm $H_2O$. A pneumatic compressor (Thumper) exerted a force of 120 N over the sternum. SEP were generated by a stimulus at the ulnar nerve. Conduction latency (LAT) and amplitude (AMP) of primary cortical wave were measured over contralateral somatosensory cortex and are reported as a percent of prearrest. Nine animals received a bolus of 1 mg EPI after fibrillating the heart followed by a constant infusion of 4 ug/kg/min. Eleven other animals received a bolus of 1 mg PE followed by an infusion of 20 ug/kg/min. CPR was continued for 20 minutes. Following a 1 meq/kg dose of sodium bicarbonate, defribrillation was attempted. If successful within four attempts, infusion of drug was weaned and discontinued and the animals were observed for 120 minutes. Measurements were made pre-arrest, and at 7 and 15 min of CPR, and 10, 60, and 120 min following cardiac resuscitation.

Results: Seven of 9 and 8 of 11 animals were successfully resuscitated in the EPI and PE groups respectively. The aortic minus right atrial diastolic pressure gradient (AORAD) was sufficient during CPR in both groups to generate MBF of 34-42 ml/min/100g. CPP, CBF, and $CMRO_2$ were equivalent in both drug groups and $CMRO_2$ was maintained at prearrest levels during CPR. At 10 minutes after resuscitation, MAP was higher in the PE group but without differences in MBF or CBF. SEP were not significantly different from prearrest LAT or AMP during CPR and following cardiac resuscitation.

Discussion: The peripheral vasoconstrictive properties of both drugs led to equivalent levels of cerebral and myocardial perfusion pressures. Thus, PE is capable of producing similar levels of CBF and MBF as EPI. Moreover, $CMRO_2$ and SEP were maintained near prearrest levels in both groups during and following CPR. This makes it unlikely that epinephrine had a major beta-stimulating effect on cerebral metabolism independent of CBF when the delay in onset of CPR is brief. Therefore, following a short ischemic period in adult dogs, PE and EPI provide similar benefits on CBF, $CMRO_2$ and MBF during CPR, thereby sustaining brain conductive function and allowing for successful resuscitation in 75% of animals.

Table 1 - EPINEPHRINE (means ± SE)

| | Pre-Arrest | 7 min | 15 min | 10 min Post | 60 min Post | 120 min Post |
|---|---|---|---|---|---|---|
| MAP | 107±5 | 64±4 | 63±4 | 79±6 | 95±6 | 96±7 |
| CPP | 97±6 | 44±3 | 45±4 | 69±6 | 90±6 | 92±7 |
| AORAD | 90±6 | 25±3 | 27±3 | 60±6 | 81±7 | 88±6 |
| MBF | 63±11 | 36±6 | 39±8 | 118±30 | 75±12 | 84±22 |
| CBF | 33±4 | 27±2 | 27±2 | 42±8 | 23±3 | 26±5 |
| $CMRO_2$ | 2.8±.3 | 3.4±.4 | 3.3±.1 | 3.0±.2 | 2.4±.2 | 2.9±.5 |
| EXT | .50±.06 | .60±.04 | .63±.04 | .50±.06 | .60±.04 | .55±.06 |
| AMP | 100±0 | 86±9 | 72±14 | 107±14 | 88±14 | 80±12 |

Table 2 - PHENYLEPHRINE (mean ± SE)

| | Pre-Arrest | 7 min | 15 min | 10 min Post | 60 min Post | 120 min Post |
|---|---|---|---|---|---|---|
| MAP | 101±5 | 64±4 | 61±2 | 127±7 | 95±5 | 90±4 |
| CPP | 92±5 | 46±4 | 43±2 | 118±7 | 88±5 | 80±4 |
| AORAD | 89±5 | 28±3 | 27±3 | 109±8 | 87±5 | 80±5 |
| MBF | 64±6 | 35±4 | 42±6 | 119±16 | 78±7 | 60±11 |
| CBF | 31±3 | 21±2 | 25±3 | 40±6 | 34±5 | 29±4 |
| $CMRO_2$ | 3.0±.3 | 2.5±.3 | 2.9±.4 | 2.9±.4 | 3.5±.4 | 3.1±.4 |
| EXT | .57±.04 | .61±.04 | .59±.05 | .44±.04 | .64±.04 | .67±.03 |
| AMP | 100±0 | 82±9 | 91±10 | 113±16 | 100±15 | 94±10 |