Effect of Adrenergic Drugs on Cerebral Blood Flow, Metabolism, and Evoked Potentials After Delayed Cardiopulmonary Resuscitation in Dogs

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Background and Purpose: Epinephrine administration during cardiopulmonary resuscitation increases cerebral blood flow by increasing arterial pressure. We tested whether potential β-adrenergic effects of epinephrine directly influence cerebral blood flow and oxygen consumption independently of raising perfusion pressure.

Methods: Four groups of seven anesthetized dogs were subjected to 8 minutes of fibrillatory arrest followed by 6 minutes of chest compression, ventricular defibrillation, and 4 hours of spontaneous circulation. Cerebral perfusion pressure was increased to approximately equivalent ranges during resuscitation by either 1) epinephrine infusion, 2) epinephrine infusion after pretreatment with the lipophylic β-adrenergic antagonist pindolol, 3) infusion of the α-adrenergic agonist phenylephrine, or 4) descending aortic balloon inflation without pressor agents.

Results: We found no difference in cerebral blood flow, oxygen extraction, or oxygen consumption during chest compression among groups. After ventricular defibrillation, depressed levels of cerebral blood flow, cerebral oxygen consumption, and somatosensory evoked potential amplitude were not different among groups.

Conclusions: We detected no evidence that after 8 minutes of complete ischemia, epinephrine administration during resuscitation substantially influences cerebral blood flow or cerebral oxygen consumption independent of its action of raising arterial pressure or that epinephrine has a negative impact on immediate metabolic or electrophysiological recovery attributable to its β-adrenergic activity. (Stroke 1991;22:1554-1561)

Epinephrine is recommended for use during cardiopulmonary resuscitation (CPR) because it increases perfusion pressure for heart and brain by preferential vasoconstriction of other vascular beds.1,2 However, epinephrine in high doses, commonly used during CPR, may also exert direct effects on brain independent of raising cerebral perfusion pressure. For example, catecholamines can stimulate cerebral O2 consumption (CMRO2) in certain experimental situations such as severe hypertension, immobilization, and hypoglycemia.3-6 Furthermore, if epinephrine gains direct access to cerebral arterioles, it may produce vasoconstriction or vasodilation depending on the balance of α- and β-adrenergic influences.7-9 In the carotid occlusion plus hypotension model of cerebral ischemia, circulating catecholamines may ameliorate neuronal damage.10

In previous work, we did not detect differences in cerebral blood flow (CBF) or CMRO2 between administration of the α-adrenergic agonist phenylephrine and administration of the mixed α- and β-adrenergic agonist epinephrine at equipotent pressor doses.11 However, in that study CPR commenced immediately upon ventricular fibrillation and the brain did not become severely ischemic. When the onset of CPR is delayed, as would ordinarily occur in practice, epinephrine might have greater access to the brain because of ischemic injury and because endothelial monoamine oxidase, which ordinarily provides a metabolic barrier to catecholamine entry, may be inhibited by tissue hypoxia.12,13 Furthermore, in our previous study no comparisons were made with...
a group receiving a β-adrenergic antagonist or a control group receiving no pressor drug to more clearly discern any β-adrenergic effects.

In the present study, we investigated the physiological effects of epinephrine administration when the institution of CPR is delayed 8 minutes in anesthetized dogs. We tested whether epinephrine administration during CPR resulted in a significant increase in CBF and CMRO₂ independent of the drug’s effect on raising cerebral perfusion pressure. Three comparisons were made. First, cerebral perfusion pressure was mechanically increased during CPR by inflation of a balloon in the descending aorta to attain the same level of cerebral perfusion pressure as that with epinephrine administration. Second, to test for β-adrenergic effects of epinephrine, the lipophylic β-receptor antagonist pindolol was administered before cardiac arrest and epinephrine infusion. Third, phenylephrine was administered to determine whether there are differences between use of an α-adrenergic agonist and a mixed α and β-adrenergic agonist. In addition, we assessed the impact of these treatments during CPR on the immediate postischemic evoked potential recovery.

Materials and Methods

Mongrel dogs ranging in weight from 18.2 to 26.8 kg were anesthetized with fentanyl (40–55 μg/kg i.v.) and pentobarbital (6 mg/kg i.v.) and were artificially ventilated through a cuffed endotracheal tube secured by a tracheostomy. Fractional inspired O₂ was 0.3–0.5 and end-tidal CO₂ was approximately 35 mm Hg. Additional anesthetics were given to maintain a sufficient depth of anesthesia for surgery. There were no differences in the cumulative amount of additional fentanyl (approximately 50 μg/kg) and pentobarbital (3–6 mg/kg/hr) administered to the different treatment groups.

Catheters were inserted through an axillary artery, two femoral arteries, and femoral and axillary veins into the subclavian artery, thoracic aorta, left ventricle, and right atrium, respectively. In one group of dogs, a balloon-tipped catheter was placed into the thoracic descending aorta. A small catheter was inserted into the superior sagittal sinus with the catheter tip approximately 1 cm anterior to the confluence of the sinuses. A straight ventricular drain catheter was placed through a burr hole into the lateral ventricle.

Dogs were placed supine on a V-shaped wooden board. Pancuronium (0.1 mg/kg) and heparin sulfate (4,000 units) were administered intravenously before induction of cardiac arrest. Ventricular fibrillation was induced by passing a 60-Hz alternating current through a 4F pacing catheter in the right heart and ventilation was stopped. After 8 minutes of arrest, CPR was instituted. Dogs were randomly assigned to four groups: 1) seven dogs received a 1-mg bolus of epinephrine into the left ventricle followed by a continuous intravenous infusion of 4 μg/kg/min; 2) seven dogs received a 1-mg bolus injection of phenylephrine into the ventricle followed by a continuous intravenous infusion of 20 μg/kg/min; 3) seven dogs were pretreated 2 hours before arrest with a subclavian arterial infusion of pindolol (2 mg/kg over 20 min), and during CPR they received epinephrine (1 mg bolus into the left ventricle plus 4 μg/kg/min, intravenously); 4) seven control dogs received no drug treatment during CPR, but instead cephalic and coronary perfusion pressures were increased by inflation of the balloon-tipped catheter (5 ml) in the descending aorta throughout CPR. All groups received intravenous saline at a rate of 7.6 ml/min during CPR. Dosage regimen of the pressor agents was based on pilot studies which indicated that phenylephrine at a rate of 20 μg/kg/min produced perfusion pressures equivalent to epinephrine at a rate of 4 μg/kg/min. These dosages result in stable perfusion pressure.²,¹¹

Sternal compressions were administered by a microprocessor-controlled pneumatic chest compressor (Thumper; Michigan Instruments, Grand Rapids, Mich.) at a rate of 40 per minute with a compression duration of 50% of the total cycle time. Compression force was set to 110–120 N to generate a cyclic sternal displacement of approximately 15–20% of the anteroposterior chest diameter. Ventilation was performed simultaneously at high airway pressures (75–95 mm Hg) with a gas mixture of 95% O₂ and 5% CO₂ to ensure adequate oxygenation and to prevent hypocapnia. Ventilation was limited to the first 40% of each compression cycle. Though not used clinically on a routine basis, simultaneous ventilation and chest compression in large dogs permits the generation of perfusion pressures that are sufficiently high for testing whether pharmacological agents alter CBF and metabolism independent of cerebral perfusion pressure.²,¹⁴ After 6 minutes of CPR, four defibrillation attempts at 200–360 J were allowed. Resuscitation was considered successful if aortic systolic pressure exceeded 75 mm Hg within 1 minute. Ventilation was adjusted to keep end-tidal CO₂ at 35–40 mm Hg. Sodium bicarbonate was given if arterial pH was less than 7.2. The infusion of epinephrine or phenylephrine was reduced incrementally, or the aortic balloon was deflated slowly, when mean aortic pressure exceeded 90 mm Hg.

Somatosensory-evoked potentials (SEP) and brain stem auditory-evoked responses were measured as previously described.¹¹,¹⁵,¹⁰ Blood gases, pH, and O₂ contents were analyzed from simultaneously obtained arterial and sagittal sinus blood.¹¹ Plasma catecholamine levels were measured by high-pressure liquid chromatography with electrochemical detection.¹¹,¹³ To measure regional blood flow, radiolabeled microspheres (16±0.5 μm diameter; Du Pont-NEN Products, Boston, Mass.) were injected into the left cardiac ventricle with dosages, withdrawal rates, and calculations as previously described.¹¹ Use of microspheres during CPR has been previously validated.¹⁴ Cerebral O₂ uptake was calculated as the
product of the difference between arterial and sagittal sinus O₂ content and blood flow to the cerebrum.

Measurements were compared between groups by use of two-way analysis of variance having a split-plot design with repeated measures over time within each group. Mean values were compared between groups using Duncan’s new multiple-range test, and within group values were compared to the prearrest control value by paired t test with Bonferroni correction. For plasma catecholamines and CBF, an arc tangent transformation was performed to reduce skewness. Values are mean±SEM, and the level of significance was p<0.05.

**Results**

With inflation of the balloon in the descending aorta, mean aortic pressure was 66±5 mm Hg at 1.5 minutes of CPR when microspheres were injected and was maintained at 5.5 minutes when the microsphere reference sampling ended (Table 1). The value in the phenylephrine group was significantly higher at 1.5 minutes, but not by 5.5 minutes. There were no other differences among groups during CPR. In addition, the peak aortic pressures during chest compression were not different among groups. After 5.5 minutes of CPR when microspheres were injected and was maintained at 5.5 minutes when the microsphere reference sampling ended (Table 1). The value in the phenylephrine group was significantly higher at 1.5 minutes, but not by 5.5 minutes. There were no other differences among groups during CPR. In addition, the peak aortic pressures during chest compression were not different among groups. After 5.5 minutes of CPR, the median number of defibrillation attempts was two in all groups. As mean aortic...
pressure recovered to prearrest levels, weaning from vasopressor support was complete in most dogs when the first set of postresuscitation measurements were made at 10 minutes. One dog in the balloon group died at 210 minutes after defibrillation.

Both intracranial and sagittal sinus pressures increased during CPR (Table 1). The increase was approximately one third that of right atrial pressure, in agreement with other studies. Plasma norepinephrine levels increased by more than one order of magnitude in all groups during CPR. Plasma epinephrine levels increased by approximately two orders of magnitude in the balloon group, whereas epinephrine infusion increased the level by an additional order of magnitude (Table 1). Arterial pH decreased from 7.37±0.02 to 7.17±0.04, 7.14±0.03, 7.20±0.04, and 7.20±0.04 during CPR in the epinephrine, phenylephrine, pindolol plus epinephrine, and balloon groups, respectively; pH returned to prearrest levels with mean cumulative administration of 2.6, 3.1, 3.3, and 1.8 meq/kg of sodium bicarbonate soon after resuscitation in the corresponding groups. There were no major changes from prearrest levels of arterial Pco2 (36±2 mm Hg), Po2 (222±16 mm Hg), or O2 content (19±1 ml/dl).

Despite the reduced cerebral perfusion pressure during CPR, CBF was not reduced in any group (Figure 1), thereby indicating cerebrovasodilation. In the pindolol plus epinephrine group, CBF was significantly greater than the prearrest level, but there were no significant differences among groups during CPR. The large SEM during CPR is attributable to one or two dogs in each group in whom CBF tripled in association with the highest level of perfusion pressure individually generated in each group. Power analysis indicated a 30% chance of failing to detect a true difference between the balloon group and either the phenylephrine or pindolol group. At 120 minutes after resuscitation, CBF decreased 30-50% below prearrest levels in all groups (Figure 1). In caudal brain regions, CBF generally increased during CPR and the increase persisted 10 minutes after resuscitation, but there were no differences among groups (Table 2). Delayed hypoperfusion was also evident in some caudal brain regions. Blood flow in pons and midbrain behaved similar to that in medulla (data not shown). Blood flow in middle and posterior cerebral artery territories and border territories were within 10% of that in whole cerebrum (data not shown).

Cerebral arteriovenous O2 content difference was unchanged during CPR from prearrest values (Table 1). There were no differences among groups during CPR or after resuscitation. During CPR, CMRO2 was maintained at prearrest levels in all groups (Figure 2). Epinephrine administration alone did not increase cerebral O2 extraction (Table 1) or CMRO2 (Figure 2) above that of the other groups during CPR. After resuscitation CMRO2 transiently decreased in all groups except with pindolol pretreatment, but there were no differences among groups.

During cardiac arrest, evoked potentials became flat. Detectable SEP were obtained at 4±1, 16±6, 7±1, and 10±4 minutes after resuscitation in the epinephrine, phenylephrine, pindolol, and balloon groups.
groups, respectively. The corresponding recovery of SEP amplitude of the primary cortical wave complex at 240 minutes was $41 \pm 13$, $26 \pm 14$, $61 \pm 16$, and $30 \pm 5\%$ of prearrest values. There were no differences among groups. Full amplitude recovery occurred in only one dog in each of the epinephrine and pindolol groups. Latencies of the wave recorded over the second cervical vertebra ($9.2 \pm 0.5$ msec) and of the first major negative wave recorded over somatosensory cortex ($20.4 \pm 0.7$ msec) returned to prearrest values. Recovery of brain stem auditory evoked responses was detected during CPR in two, three, two, and five of the seven dogs in the epinephrine, phenylephrine, pindolol, and balloon groups, respectively. Latencies of the first through fifth waves generally recovered in all dogs by 10 minutes after resuscitation.

During CPR the pressure gradient between aorta and right atrium was sufficient to maintain coronary blood flow at prearrest levels (Table 3). The ratio of subendocardial to subepicardial left ventricular blood flow fell during CPR in the epinephrine group (1.25±0.06 to 0.79±0.09), but was not significantly changed in the phenylephrine (1.24±0.10 to 1.00±0.11), pindolol (1.15±0.05 to 0.91±0.14), and balloon (1.24±0.05 to 0.99±0.08) groups. After defibrillation, mean and transmural ventricular blood flow at prearrest levels (Table 3). The ratio of subendocardial to subepicardial left ventricular blood flow fell during CPR in the epinephrine, pindolol, and balloon groups, respectively. Latencies of the first through fifth waves generally recovered in all dogs by 10 minutes after resuscitation.

These results indicate that increasing cerebral perfusion pressure during CPR either by mechanical means with a balloon in the aorta or by administration of the $\alpha$-adrenergic agonist phenylephrine produces a level of CBF, $O_2$ extraction, and CMRO$_2$ equivalent to that produced by epinephrine both in the absence and presence of $\beta$-adrenergic blockade. Furthermore, recovery of CBF, CMRO$_2$, and SEP after resuscitation was equivalent in all four groups. Therefore, within the limits of our experimental design and measurements, we found no evidence that epinephrine administration by virtue of its $\beta$-adrenergic properties causes additional cerebral vasodilation or $O_2$ uptake during CPR, nor does epinephrine administration during CPR have an adverse impact upon delayed hypoperfusion, depressed CMRO$_2$, or evoked potential recovery.

One would anticipate that neurohumoral modulation of CBF would be diminished after ischemia because of the local release of multiple vasodilatory substances. However, Moskowitz et al$^{20}$ suggest that nerves, albeit nonsympathetic nerves, are capable of modifying postischemic hyperemia. We found that epinephrine infusion increased plasma levels approximately 10-fold over that in the control group with aortic balloon inflation, but that CBF was similar over an equivalent range of cerebral perfusion pressure. This observation indicates that the additional circulating epinephrine did not have a major influence on cerebrovascular tone unless $\alpha$- and $\beta$-adrenergic effects were offsetting. However, our observation that CBF was not lower with pindolol pretreatment or with phenylephrine administration makes it unlikely that epinephrine administration causes $\beta$-adrenergic vasodilation or that $\beta$-adrenergic vasodilation masks $\alpha$-adrenergic vasoconstriction during CPR. Alternatively, $\beta$-adrenergic cerebrovasodilation may simply be less prominent in the dog than in other species.$^{20}$ However, during hemorrhage

<table>
<thead>
<tr>
<th>Region/Group</th>
<th>Prearrest</th>
<th>CPR 73±16*</th>
<th>CPR 74±16*</th>
<th>CPR 75±16*</th>
<th>CPR 76±16*</th>
<th>Prearrest</th>
<th>CPR 73±16*</th>
<th>CPR 74±16*</th>
<th>CPR 75±16*</th>
<th>CPR 76±16*</th>
<th>Prearrest</th>
<th>CPR 73±16*</th>
<th>CPR 74±16*</th>
<th>CPR 75±16*</th>
<th>CPR 76±16*</th>
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<tbody>
<tr>
<td>Cerebellum</td>
<td>Epinephrine 40±3</td>
<td>73±16*</td>
<td>59±10</td>
<td>31±3</td>
<td>20±2*</td>
<td>23±3*</td>
<td>Phenylephrine 36±3</td>
<td>95±13*</td>
<td>114±23*</td>
<td>30±5</td>
<td>24±2</td>
<td>26±2</td>
<td>Phenylephrine 32±2</td>
<td>103±18*</td>
<td>57±7*</td>
</tr>
<tr>
<td>Medulla</td>
<td>Epinephrine 27±3</td>
<td>70±14*</td>
<td>69±11*</td>
<td>22±2</td>
<td>16±3</td>
<td>19±2</td>
<td>Phenylephrine 25±2</td>
<td>109±18*</td>
<td>78±19*</td>
<td>21±2</td>
<td>18±1</td>
<td>21±2</td>
<td>Pindolol + epi 20±2</td>
<td>110±20*</td>
<td>88±14*</td>
</tr>
<tr>
<td>Diencephalon</td>
<td>Epinephrine 33±3</td>
<td>69±18*</td>
<td>64±14</td>
<td>23±2</td>
<td>18±2*</td>
<td>22±2</td>
<td>Phenylephrine 34±3</td>
<td>92±13*</td>
<td>75±15*</td>
<td>24±3</td>
<td>23±1*</td>
<td>27±1</td>
<td>Pindolol + epi 26±2</td>
<td>99±16*</td>
<td>77±8*</td>
</tr>
</tbody>
</table>

Values are mean±SEM in ml/min/100 g. CPR, cardiopulmonary resusitation; epi, epinephrine. *p<0.05 vs. prearrest value.
in hypoglycemic dogs increases in CBF and CMRO$_2$ can be blocked by combined propranolol and phentolamine treatment, suggesting a metabolic and vasodilatory adrenergic influence in canine brain.

In cats, Nemoto et al. found that propranolol treatment blunted the decrease in O$_2$ extraction during postischemic hyperemia and suggested that $\beta$-adrenergic receptors contribute to postischemic vasodilation. With pindolol treatment, we observed no such differences during CPR or 10 minutes after defibrillation. Whether this represents a species difference or a difference in the experimental model, anesthesia, or use of pindolol rather than propranolol is unclear. We chose to use pindolol as a lipophilic $\beta$-adrenergic antagonist accessible to the brain because propranolol may exert membrane-stabilizing effects that could influence the results. Although pindolol can exert a partial agonist effect when sympathetic activity is low, we did not observe increases in heart rate prior to arrest.

Epinephrine administration in doses sufficient to produce hypertension-induced blood–brain barrier disruption in nonischemic rats causes increases in CBF and CMRO$_2$. Furthermore, increases in CBF and CMRO$_2$ associated with immobilization stress are blocked by propranolol or adrenalectomy. Thus, high circulating levels of epinephrine during CPR could potentially cause increases in CMRO$_2$. However, we did not find greater levels of CMRO$_2$ or O$_2$ extraction during CPR with epinephrine infusion than with phenylephrine infusion, epinephrine infusion with pindolol pretreatment, or no drug infusion in the balloon group. Thus, we found no evidence that high-dose epinephrine infusion during CPR stimulates CMRO$_2$ after an 8-minute period of cardiac arrest. This conclusion is supported by the finding that epinephrine-induced increases in cerebral perfusion pressure during open-chest CPR are accompanied by decreases in cerebral O$_2$ extraction with no change in CMRO$_2$.

One explanation for these negative results is that endogenous release of central and peripheral catecholamines as a consequence of ischemia may have already elicited the maximum adrenergic effect. However, our observation that pindolol pretreatment did not result in lower CBF after arrest suggests that $\beta$-adrenoceptors do not play a major role in postischemic vasodilation or in stimulating CMRO$_2$ immediately after ischemia. Influence of the catecholaminergic system may be overshadowed by the complex metabolic alterations occurring immediately after ischemia and by the action of other neurotrans-

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**Table 3. Organ Blood Flow Before, During, and After Resuscitation**

<table>
<thead>
<tr>
<th>Group</th>
<th>Prearrest</th>
<th>CPR</th>
<th>Postresuscitation (min)</th>
</tr>
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<tbody>
<tr>
<td></td>
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<td>10</td>
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<td></td>
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<td>120</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>240</td>
</tr>
<tr>
<td><strong>Left ventricle</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epinephrine</td>
<td>68±12</td>
<td>71±19</td>
<td>90±38</td>
</tr>
<tr>
<td>Phenylephrine</td>
<td>49±12</td>
<td>120±29</td>
<td>77±14</td>
</tr>
<tr>
<td>Pindolol + epi</td>
<td>63±11</td>
<td>98±14</td>
<td>41±1</td>
</tr>
<tr>
<td>Balloon</td>
<td>68±12</td>
<td>51±6</td>
<td>65±8</td>
</tr>
<tr>
<td><strong>Kidney</strong></td>
<td></td>
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</tr>
<tr>
<td>Epinephrine</td>
<td>450±43</td>
<td>7±3*</td>
<td>149±45*</td>
</tr>
<tr>
<td>Phenylephrine</td>
<td>383±37</td>
<td>16±4*</td>
<td>142±27*</td>
</tr>
<tr>
<td>Pindolol + epi</td>
<td>425±20</td>
<td>3±1*</td>
<td>141±24*</td>
</tr>
<tr>
<td>Balloon</td>
<td>413±24</td>
<td>5±2*</td>
<td>232±47</td>
</tr>
<tr>
<td><strong>Jejunum</strong></td>
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<td></td>
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<tr>
<td>Epinephrine</td>
<td>25±5</td>
<td>1±1*</td>
<td>16±3</td>
</tr>
<tr>
<td>Phenylephrine</td>
<td>23±2</td>
<td>10±3*</td>
<td>24±4</td>
</tr>
<tr>
<td>Pindolol + epi</td>
<td>23±3</td>
<td>3±1*</td>
<td>18±1</td>
</tr>
<tr>
<td>Balloon</td>
<td>30±6</td>
<td>5±1*</td>
<td>30±5</td>
</tr>
<tr>
<td><strong>Tongue</strong></td>
<td></td>
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<tr>
<td>Epinephrine</td>
<td>5.4±1.2</td>
<td>0.1±0.02*</td>
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<td>Phenylephrine</td>
<td>3.7±0.6</td>
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<tr>
<td>Pindolol + epi</td>
<td>5.6±1.7</td>
<td>0.1±0.03*</td>
<td>5.5±1.7</td>
</tr>
<tr>
<td>Balloon</td>
<td>5.7±1.2</td>
<td>0.4±0.14*</td>
<td>4.6±1.5</td>
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<td><strong>Cephalic muscle</strong></td>
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<td>Epinephrine</td>
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<td>Balloon</td>
<td>8.3±4.1</td>
<td>1.1±0.29*</td>
<td>6.0±2.1</td>
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</table>

Values are mean±SEM in ml/min/100 g. CPR, cardiopulmonary resusitation.

* $p<0.05$ vs. prearrest value; † $p<0.05$ vs. pindolol + epi (epinephrine) group; ‡ $p<0.05$ vs. epinephrine group.
matters. In addition, because of transient increases in O₂ uptake upon reoxygenation, individual dogs may not have been in a sufficient steady state of O₂ uptake to permit statistical detection of differences among groups during CPR.

Another explanation is that circulating epinephrine does not cross the blood–brain barrier during CPR. This explanation is supported by our previous finding that the brain transfer coefficient of aminoxybutyric acid is not increased in this experimental model of CPR. Nevertheless, even if the blood–brain barrier is not disrupted, epinephrine might cross the barrier if endothelial monoamine oxidase activity is inhibited by low P/O during initial reperfusion or if energy-dependent catecholamine uptake is inhibited by ischemia. However, Wortsman et al reported no increases in cerebrospinal fluid levels of epinephrine during CPR. This finding suggests that the enzymatic barrier is not functionally impaired during CPR.

We also examined whether use of high-dose epinephrine during CPR would have a negative effect on immediate cerebral recovery. However, we found that the degree of CBF, CMRO₂, and SEP amplitude reductions below prearrest values were not different in the epinephrine group than in the other groups. Thus, use of epinephrine during CPR does not appear to affect immediate metabolic or electrophysiological recovery. Moreover, Brillman et al found no difference in neurological recovery between epinephrine and phenylephrine treatment during CPR after 3 minutes of arrest in dogs.

The magnitude of the reduction of CBF (54%), CMRO₂ (37%), and SEP amplitude (54%) below prearrest values at 120 minutes after resuscitation in the epinephrine group with 8 minutes of complete ischemia is similar to that previously reported from this laboratory in which 12 minutes of complete ischemia was produced by intracranial hypertension in dogs (32%, 22%, and 62%, respectively) and in which 10 minutes of complete ischemia was produced by aortic cross-clamp in pigs (42%, 20%, and 68%, respectively). In contrast, when ischemic duration was minimized by instituting CPR immediately upon confirmation of ventricular fibrillation, CBF, CMRO₂, and SEP were sustained at prearrest levels after defibrillation. Thus, application of CPR with adequate levels of cerebral perfusion pressure does not appear to produce any additional decrements in cerebral hemodynamic, metabolic, or electrophysiological parameters beyond that expected from the delay in starting CPR after arrest.

In contrast to SEP, brain stem auditory evoked responses rapidly recovered after resuscitation consistent with the concept that brain stem function is more resistant to transient ischemia than forebrain function. Whether rapid recovery of the auditory response is related to the marked brain stem hyperemia during CPR and 10 minutes after resuscitation is unclear. In other stresses such as hypoxia and immobilization, a caudal redistribution of blood flow is thought to be adrenergically mediated. However, we found that brain stem hyperemia remained prominent with pindolol treatment, suggesting a non-β-adrenergic mechanism.

The near-normal levels of CBF concomitant with near-zero levels of blood flow in extracranial cerebral tissues with epinephrine or phenylephrine infusion during CPR are consistent with the concept that α-adrenergic sensitivity in intracranial arterioles is much less than in extracranial arterioles. Little data are available on peripheral organ blood flow after resuscitation. Our data show that other than brain, delayed hypoperfusion was significant only in kidney. In left ventricle, the ratio of subendocardial to subepicardial blood flow decreased during CPR as observed previously, but the ratio and total flow recovered after resuscitation.

In summary, we found no evidence that use of high-dose epinephrine during CPR after a period of 8 minutes of cardiac arrest exerts any direct effect on CBF or CMRO₂ independent of the drug’s effect on raising cerebral perfusion in otherwise normal healthy dogs. Whether these observations would hold true in the presence of underlying cardiovascular disease is uncertain. Furthermore, although we found no difference in immediate metabolic and electrophysiological recovery, we cannot discount more long-term histological or neurological effects associated with use of epinephrine.

Acknowledgments

The authors express their gratitude to Dr. Kenneth Kubos for performing the catecholamine assay, to Ms. Karen Dwyer for her valuable technical assistance, and to Lisa DeLoriers and Candace Berryman for their assistance in preparing the manuscript.

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KEY WORDS • cerebral blood flow • epinephrine • resuscitation • dogs
Effect of adrenergic drugs on cerebral blood flow, metabolism, and evoked potentials after delayed cardiopulmonary resuscitation in dogs.
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Stroke. 1991;22:1554-1561
doi: 10.1161/01.STR.22.12.1554

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/22/12/1554