Cerebral and systemic circulatory effects of arterial hypotension induced by adenosine

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In six dogs anesthetized with halothane and nitrous oxide, mean arterial pressure (MAP) was lowered to 40 mm Hg for an average of 90 minutes by intravenous infusion of adenosine. The hypotensive effect of the adenosine was potentiated by administering dipyridamole to block its intravascular inactivation. Blood flow to the brain, spinal cord, heart, kidneys, and skeletal muscle was measured six times in each animal using the radioactive microsphere technique. Determinations were made before, during, and 30 minutes after the hypotensive period.

During the hypotensive period, MAP was decreased 61% and was related to a proportional decrease in peripheral vascular resistance. Cardiac index decreased 14%. Total cerebral blood flow (CBF) decreased an average of 28% and cerebral vascular resistance decreased 53%. The reduction in CBF was heterogeneous; the cerebral cortex and corpus callosum were most affected and the brain stem least affected. No change occurred in the cerebral metabolic rate of oxygen usage (CMRO2). Left ventricle flow increased 147% and right ventricle flow increased 271%. Blood flow to the kidneys decreased 70%, and to the liver decreased to 6% of control. Jejunum blood flow increased 138% during recovery, while stomach flow varied but showed no statistical change. There was no tachyphylaxis, rebound hypertension, or toxicity associated with the adenosine-induced hypotension. These properties suggest that adenosine may be a useful agent for inducing arterial hypotension in neurosurgical patients.

KEY WORDS □9 adenosine □9 arterial hypotension □9 blood flow □9 dipyridamole

INDUCED arterial hypotension is commonly employed in neurosurgical practice to facilitate operations for aneurysms, arteriovenous malformations, and vascular tumors. Furthermore, it is used in certain centers in an attempt to decrease the incidence of aneurysmal rebleeding in the preoperative period. The most frequently used agents for inducing arterial hypotension include nitroprusside, nitroglycerin, trimethaphan, and halothane (intraoperatively). These agents all suffer from one or more of the following disadvantages: cyanide toxicity, rebound hypertension, decreased cardiac output, tachyphylaxis, and excessive cerebral vasodilation.

Adenosine is a naturally occurring substance found ubiquitously in all body tissues. Given intravenously in pharmacological doses, it is a potent vasodilator in most vascular beds and readily produces profound reductions in arterial pressure. The purpose of this study was to document the cerebral and systemic vascular effects of parenterally administered adenosine in an attempt to determine its potential as a clinical agent for inducing arterial hypotension.

Materials and Methods

Six mongrel dogs, weighing approximately 15 kg each, were used for this study. The animals were anesthetized with 0.5% halothane in 70% nitrous oxide and 30% O2. Muscular paralysis was achieved with pancuronium, 0.2 mg/kg given intravenously, supplemented as necessary. The animals were ventilated with a Harvard pump respirator, and CO2 was added to the inspired gas mixture to maintain arterial pCO2 at 40 mm Hg. Temperature was measured from a Swan-Ganz thermistor and maintained at 37°C with a heating blanket.

* Harvard pump respirator manufactured by Harvard Apparatus, Inc., 150 Dover Mills Road, Millis, Massachusetts.
† Swan-Ganz thermistor manufactured by Edwards Laboratories, 17221 Red Hill Avenue, Santa Ana, California.
Systemic arterial pressure was monitored from a catheter introduced into the aorta through the brachial artery. Sagittal sinus pressure was measured from a catheter placed in the anterior sagittal sinus and directed caudally into the posterior third of the sinus. Pulmonary artery wedge and central venous pressures, as well as cardiac output (using the thermodilution technique), were measured from a Swan-Ganz catheter inserted through the femoral vein. Left ventricle end diastolic pressure was measured using a pigtail catheter inserted retrogradely through the femoral artery. The position of the pigtail catheter in the left ventricle was confirmed by observing the waveform of the monitored pressure. Heart rate was derived from the electrocardiogram. End-tidal CO₂ was measured continuously with a Hewlett-Packard 47210A capnometer. These physiological parameters were recorded continuously on a Hewlett-Packard 7758B eight-channel strip chart recorder. Electroencephalograms (EEG's) were obtained from four needle electrodes placed in the scalp and recorded on a Grass Model 8-10 C electroencephalograph.

Blood flow to the brain and spinal cord, right and left ventricles of the heart, liver, kidney, stomach, jejunum, and temporalis and paraspinous muscles was measured using the radioactive microsphere technique. Regions of the central nervous system studied were the cortical gray matter, mixed white and gray matter samples from the right and left hemispheres, the corpus callosum, the right and left caudate nuclei, the brain stem, cerebellum, and the cervical and thoracic spinal cord. In each animal, six determinations of blood flow were made using 15 ± 5 μ carbonized spheres labeled with iodine-125, cerium-141, strontium-85, niobium-95, scandium-46, or gadolinium-153. The microspheres were injected into the left ventricle through the pigtail catheter. Femoral and brachial artery reference samples were drawn at a rate of 1.03 ml/min for 30 seconds before and 3.89 minutes after injection of the microspheres. The blood and tissue were counted in a Packard Auto-Gamma scintillation spectrometer. Immediately before each blood flow measurement, blood was drawn for determination of arterial blood gases, hematocrit, and oxygen content of arterial and cerebral venous (sagittal sinus) blood.

Cardiac index was estimated by dividing the cardiac output by the animal's weight. Cardiac work was calculated by multiplying the difference between the mean arterial and left ventricle end diastolic pressures by the stroke volume × 1.33 × 10⁻³. Cerebral metabolic rate of oxygen usage (CMRO₂) was estimated by multiplying the difference between the arterial and sagittal sinus oxygen content by the mean cerebral hemisphere blood flow. Cerebral perfusion pressure was calculated as the difference between the mean arterial and sagittal sinus pressure. Cerebral vascular resistance was calculated by dividing the cerebral perfusion pressure by the total mean cerebral blood flow (CBF). Peripheral vascular resistance was calculated by dividing the difference between the mean arterial and central venous pressures by the cardiac index. Hypotension was induced by infusing a solution of adenosine, 0.4 gm/100 ml normal saline, at an average dose of approximately 3 mg/kg/hr. Dipyridamole, 1 mg/kg as a loading dose supplemented by 0.5 mg/kg every 30 minutes, was used to enhance the hypotensive effect of adenosine.

Blood flow and the other physiological and biochemical parameters were determined in the control state. 15 minutes after administration of the 1-mg/kg loading dose of dipyridamole ("dipyridamole period"), at approximately 30-minute intervals after blood pressure was lowered to a mean of 40 mm Hg ("hypotensive period") with a continuous infusion of adenosine supplemented with dipyridamole, 0.5 mg/kg every 30 minutes and 30 minutes after discontinuation of the adenosine infusion ("recovery period"). The results are discussed in terms of the latter three periods: the dipyridamole, hypotensive, and recovery periods, and the changes are presented as a percentage of control values. The values for the hypotension period were obtained by averaging the three measurements taken at approximately 30-minute intervals during adenosine infusion. Statistical analysis of the data where necessary was performed using the pooled t-test. Differences were considered significant where p ≤ 0.05. Blood flow values are expressed in ml/100 gm/min.

**Results**

**Dipyridamole Period**

Administration of dipyridamole in a dose of 1 mg/kg resulted in average reductions in mean arterial pressure (MAP) of 20% and peripheral vascular resistance of 32%. There was no significant change in heart rate or cardiac index, but stroke volume increased 20% (Table 1 and Fig. 1). Myocardial flow increased dramatically: 380% in the right ventricle and 73% in the left ventricle. Renal blood flow was not changed. Blood flow to the liver and stomach decreased 64% and 62%, while jejunum flow increased 26% (Table 2 and Fig. 2).

The CMRO₂ did not change significantly. Cerebral vascular resistance decreased 27% while total brain blood flow remained unaffected (Table 3 and Figs. 3 and 4). Cervical and thoracic cord flow did not change significantly (Table 4). There was no significant var-

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**TABLE 1**

*Changes in systemic circulatory parameters*

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control Levels</th>
<th>Dipyridamole Hypotensive Period</th>
<th>Recovery Period</th>
</tr>
</thead>
<tbody>
<tr>
<td>heart rate (beats/min)</td>
<td>128 ± 6</td>
<td>122 ± 8</td>
<td>90 ± 9‡</td>
</tr>
<tr>
<td>MAP (mm Hg)</td>
<td>105 ± 6</td>
<td>84 ± 4†</td>
<td>39 ± 1§</td>
</tr>
<tr>
<td>CI (cardiac output/kg)</td>
<td>0.12 ± 0.01</td>
<td>0.12 ± 0.02</td>
<td>0.09 ± 0.02</td>
</tr>
<tr>
<td>PVR (MAP-CVP)/CI</td>
<td>8.9 ± 1.1</td>
<td>6.1 ± 0.9</td>
<td>3.4 ± 0.7†</td>
</tr>
<tr>
<td>SV (cc)</td>
<td>14.2 ± 2</td>
<td>17 ± 2</td>
<td>14 ± 2</td>
</tr>
<tr>
<td>CW (MAP-LVEDP) × SV × 1.33 × 10⁻³</td>
<td>1.8 ± 0.3</td>
<td>1.7 ± 0.2</td>
<td>0.6 ± 0.1‡</td>
</tr>
<tr>
<td>SSP (mm Hg)</td>
<td>9 ± 1</td>
<td>10 ± 1</td>
<td>10 ± 1</td>
</tr>
<tr>
<td>PAWP (mm Hg)</td>
<td>11 ± 1</td>
<td>12 ± 1</td>
<td>11 ± 1</td>
</tr>
<tr>
<td>LVEDP (mm Hg)</td>
<td>11 ± 1</td>
<td>10 ± 1</td>
<td>10 ± 1</td>
</tr>
<tr>
<td>PAP (mm Hg)</td>
<td>17 ± 1</td>
<td>19 ± 2</td>
<td>16 ± 1</td>
</tr>
<tr>
<td>CVP (mm Hg)</td>
<td>8 ± 1</td>
<td>8 ± 1</td>
<td>10 ± 1</td>
</tr>
</tbody>
</table>

* For an explanation of the three time periods, see text. Values are mean ± standard error of the mean. MAP = mean arterial pressure; CI = cardiac index; PVR = peripheral vascular resistance; SV = stroke volume; CW = cardiac work; SSP = sagittal sinus pressure; PAWP = pulmonary artery wedge pressure; LVEDP = left ventricle end diastolic pressure; PAP = pulmonary artery pressure; CVP = central venous pressure. Significance: † = p < 0.05; § = p < 0.01; ‡ = p < 0.001.

Hypotensive Period

Hypotension to a level of 40 mm Hg represented a 61% reduction in MAP. The dose of adenosine required to achieve and maintain this level was between 2.06 and 4.42 mg/kg/hr in different animals and averaged 3.02 ± 0.38 (SEM) mg/kg/hr. Hypotension was maintained for 70 to 130 minutes, with an average of 93 ± 8 minutes. No tachyphylaxis occurred during the administration of adenosine.

During hypotension, peripheral vascular resistance was lowered by 61%, heart rate decreased by 33%, and cardiac index was reduced by 14%. Stroke volume increased by 28% and cardiac work decreased 59% (Table 1 and Fig. 1). Right ventricle blood flow increased 271% and left ventricle flow 147%. Kidney blood flow decreased 70% and liver flow was decreased 87%, while stomach flow decreased 60% and jejunum flow was increased 28% (Table 2 and Fig. 2).

The CMRO₂ did not change significantly. Cerebral vascular resistance decreased 53% and total brain flow decreased 28% (Table 3 and Fig. 3). The reduction in CBF was not homogeneous; flow decreased in the cerebral cortex by 31%, in the corpus callosum by 38%, in the caudate by 29%, and in the cerebellum by 22%. The brain stem was essentially unaffected. Thoracic spinal cord flow decreased 26%, while the cervical cord flow increased 14% (Table 4 and Fig. 3).

Hematocrit and arterial pO₂ and pCO₂ were unchanged, except for a slight elevation of pCO₂ at 60 minutes of hypotension. A significant metabolic acidosis developed, as demonstrated by a reduction in arterial pH from a 7.33 ± 0.01 control level to 7.25 ± 0.01 in the recovery period, and a decrease in HCO₃⁻ from 17 ± 1 to 14 ± 1 at the same periods (Table 5). During the hypotensive period, the EEG showed no variation from the control state.

Recovery Period

Thirty minutes after discontinuation of the adenosine infusion, MAP had returned to the control level without rebound. Cardiac index, however, increased to approximately 127% of control, and peripheral vascular resistance remained approximately 27% be-

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![Fig. 1. Cardiovascular parameters in six anesthetized dogs undergoing profound arterial hypotension induced by adenosine potentiated with dipyridamole. There is a very small drop in mean arterial pressure (MAP) and peripheral vascular resistance (PVR) with dipyridamole alone. The heart rate, MAP, cardiac work, and PVR are all reduced during the adenosine infusion, while cardiac index (C.I.) remained stable. LVEDP = left ventricular end diastolic pressure; SV = stroke volume; CVP = central venous pressure. *** = p ≤ 0.001.](image-url)
Changes in organ blood flow (ml/100 gm/min)*

<table>
<thead>
<tr>
<th>Blood Flow Region</th>
<th>Control Levels</th>
<th>Dipyridamole Period</th>
<th>Hypotension Period</th>
<th>Recovery Period</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>30 Min</td>
<td>60 Min</td>
<td>90 Min</td>
<td></td>
</tr>
<tr>
<td>Lt ventricle</td>
<td>78 ± 26</td>
<td>135 ± 63</td>
<td>152 ± 59</td>
<td>134 ± 12</td>
</tr>
<tr>
<td>rt ventricle</td>
<td>41 ± 8</td>
<td>197 ± 147</td>
<td>147 ± 26‡</td>
<td>150 ± 41‡</td>
</tr>
<tr>
<td>kidney</td>
<td>440 ± 42</td>
<td>446 ± 60</td>
<td>128 ± 17§</td>
<td>290 ± 34§</td>
</tr>
<tr>
<td>liver</td>
<td>31 ± 7</td>
<td>11 ± 7</td>
<td>7 ± 3‡</td>
<td>2 ± 1‡</td>
</tr>
<tr>
<td>temp. muscle</td>
<td>4 ± 1</td>
<td>3 ± 1</td>
<td>4 ± 2</td>
<td>11 ± 6</td>
</tr>
<tr>
<td>parasp. muscle</td>
<td>6 ± 2</td>
<td>4 ± 1</td>
<td>4 ± 1</td>
<td>5 ± 1</td>
</tr>
<tr>
<td>stomach</td>
<td>41 ± 21</td>
<td>15 ± 5</td>
<td>12 ± 2</td>
<td>34 ± 8</td>
</tr>
<tr>
<td>jejunum</td>
<td>43 ± 7</td>
<td>54 ± 13</td>
<td>45 ± 4</td>
<td>102 ± 14‡</td>
</tr>
<tr>
<td>cervical sp. cord</td>
<td>28 ± 4</td>
<td>29 ± 4</td>
<td>31 ± 8</td>
<td>22 ± 2</td>
</tr>
<tr>
<td>thoracic sp. cord</td>
<td>27 ± 5</td>
<td>29 ± 6</td>
<td>20 ± 4</td>
<td>27 ± 3</td>
</tr>
<tr>
<td>total brain</td>
<td>68 ± 6</td>
<td>71 ± 8</td>
<td>46 ± 6†</td>
<td>56 ± 8</td>
</tr>
</tbody>
</table>

* For an explanation of the three time periods, see text. Values are mean ± standard error of the mean. Significance: † = p < 0.05; ‡ = p < 0.01; § = p ≤ 0.001.

low the initial value. Heart rate increased to just above the control value, while stroke volume and cardiac work were increased 22% and 23%, respectively (Table 1 and Fig. 1). Right ventricle and left ventricle blood flows decreased slightly from the high levels noted during the hypotensive period, still remaining considerably elevated from control values. During recovery, the right ventricle blood flow was 226% of control and the left ventricle flow was 72% of control. Renal blood flow approximately doubled from the hypotensive level but still remained 34% below control. Stomach blood flow approximated control values, while liver flow was decreased 94%. Jejunum flow increased markedly, reaching 238% of control (Table 2 and Fig. 2).

The CMRO2 remained unchanged from control values (Table 3 and Fig. 4). Total CBF increased from hypotensive levels but still remained 18% below control with proportional increases in flow to the different regions of the brain (Table 4 and Fig. 3). After the hypotensive period, there was a tendency toward reversal of the metabolic acidosis (Table 5).

**Discussion**

Adenosine is a potent vasodilator in most organs, acting as an inhibitory modulator of the adrenergic innervation of vascular smooth muscle. There may also be adenosine receptors providing a direct vasodilator effect and modulation of cyclic adenosine monophosphate (AMP) levels.9,16,23,27,29,33,44,48,50,53,56,58

The degree of adenosine-related vasodilation varies quantitatively in different organs, but is especially marked on the coronary circulation.9,27,33,34,40,49,52 In contrast, adenosine is a renal vasoconstrictor.23,36,47,54,59

Adenosine has been implicated as the active agent in the cerebral vasodilatory component of autoregulation to arterial hypotension, hypoxia, and hypoglycemia.18,62,64 It does not appear to cross the blood-brain barrier in significant amounts.24,32,63 When administered intravascularly, adenosine has minimal effect on the cerebral vasculature but results in a marked degree of cerebral vasodilation when added to the cerebrospinal fluid by cisternal injection.6,61

Adenosine has an intravascular half-life of approximately 15 seconds. It is rapidly inactivated by phosphorylation or deamination after being taken up by cells, particularly red blood cells.6

The aqueous solubility of adenosine is low. At room temperature a maximum of between 0.4 and 0.5 gm can be dissolved in 100 ml of water or normal saline. In our laboratory in a pilot study using dogs, hypo-
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TABLE 3
Changes in cerebral blood flow, vascular resistance, and metabolism*

<table>
<thead>
<tr>
<th>Parameters (total brain)</th>
<th>Control Levels</th>
<th>Dipyridamole Period</th>
<th>Hypotensive Period</th>
<th>Recovery Period</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>30 Min</td>
<td>60 Min</td>
</tr>
<tr>
<td>CBF (ml/100 gm/min)</td>
<td>68 ± 6</td>
<td>71 ± 8</td>
<td>46 ± 6†</td>
<td>61 ± 14</td>
</tr>
<tr>
<td>CVR</td>
<td>1.5 ± 0.3</td>
<td>1.1 ± 0.1</td>
<td>0.7 ± 0.1†</td>
<td>0.6 ± 0.1†</td>
</tr>
<tr>
<td>CMRO₂</td>
<td>3.4 ± 0.4</td>
<td>4.3 ± 0.3</td>
<td>4.4 ± 0.6</td>
<td>5.2 ± 0.7†</td>
</tr>
</tbody>
</table>

* For an explanation of the three time periods, see text. Values are mean ± standard error of the mean. CBF = cerebral blood flow; CVR = cerebral vascular resistance ((mean arterial pressure - sagittal sinus pressure)/total brain blood flow); CMRO₂ = cerebral metabolic rate of oxygen usage. Significance: † = p ≤ 0.05; ‡ = p ≤ 0.01.


dression to an MAP of 40 mm Hg could be readily induced and maintained with an infusion of adenosine, 0.4 gm/100 ml normal saline, at a dose of approximately 600 mg/kg/hr. However, this created a fluid load in excess of 100 ml/kg/hr. In order to decrease this fluid load in the current study, dipyridamole was administered to potentiate the effect of the adenosine.

Dipyridamole is a drug best known clinically for its anti-thrombotic effects. However, it is also a vasodilator with particularly marked effects on the coronary circulation. The vasodilatory properties of dipyridamole result principally from its ability to increase the circulating levels of adenosine by inhibiting the membrane-bound active transport mechanism for adenosine in most tissues (particularly blood) and thus retard its inactivation. The circulatory effects of dipyridamole observed in this study were consistent with those reported elsewhere, and will not be commented upon further. After administration of dipyridamole, there was a reduction of approximately two orders of magnitude in the dose of adenosine required to reduce MAP to 40 mm Hg. This enabled the desired level of hypotension to be maintained with a minimal fluid load. Parenthetically, it should be noted that dogs are notoriously difficult animals in which to pharmacologically induce hypotension and we speculate that adenosine alone, without the potentiating effects of dipyridamole, may be sufficient to produce hypotension in higher primates and man without involving excessive volumes of fluid.

In this study, MAP was lowered approximately 60%, to 40 mm Hg. The reduction in MAP was mostly related to the decrease in peripheral vascular resistance, with only a small concomitant reduction in cardiac output. Hypotension resulted in a progressive metabolic acidosis which reversed upon restoration of MAP to control levels. This metabolic acidosis presumably resulted from the decreased peripheral perfusion with an accumulation of acid metabolites.

![Fig. 3. Regional cerebral blood flows (cc/100 gm/min) as measured by radioactive microspheres in six anesthetized dogs during profound arterial hypotension induced with adenosine potentiated with dipyridamole. * = p ≤ 0.05; ** = p ≤ 0.01.](image)

![Fig. 4. Cerebral blood flow, metabolism, and vascular resistance in six anesthetized dogs during profound arterial hypotension induced by adenosine potentiated with dipyridamole. CMRO₂ = cerebral metabolic rate of oxygen; MAP = mean arterial pressure; SSP = sagittal sinus pressure; CBF = cerebral blood flow. *** = p ≤ 0.001.](image)
The reduction in MAP of approximately 60% was associated with a disproportionate reduction in renal blood flow of approximately 70%. The kidney has an effective autoregulatory mechanism for preserving its blood flow in hypotensive situations. In a study of hypotension produced with trimethaphan, a 60% reduction in MAP to 40 mm Hg was associated with a fall in renal flow of only 31% (Kassell NF: unpublished data). However, adenosine has a vasoconstrictor effect on the kidney, in contrast to its vasodilator actions on most other organs.23,37,47,54,59 Although renal blood flow increased after discontinuation of the adenosine infusion, it remained substantially below control levels. No explanation is available for this observation, although some residual effect of the dipyridamole may have been present when the recovery determination was made.

Liver blood flow demonstrated a gradual decline throughout the experiment. This is a nonspecific change seen with a variety of anesthetic agents and is not directly attributable to adenosine.90 Stomach blood flow varied considerably, but the changes never reached statistical significance, while the jejunum showed little change until flow more than doubled during recovery. The reason for this change in blood flow to the jejunum is unclear.

Infusion of adenosine increased myocardial flow considerably, even though systemic arterial pressure was decreased. This was in part related to the direct coronary dilatory effect of adenosine, but was also probably due to the reduction in after-load demonstrated by a decrease in cardiac work of approximately 60%, while stroke volume increased approximately 30%. Heart rate decreased 30% and stayed down throughout the period of hypotension. This effect is probably a direct inhibitory action of adenosine on the conducting system of the heart.4

Cerebral autoregulation appeared to be relatively intact in these animals. There was no change in total CBF after the 20% reduction in MAP from the loading dose of dipyridamole, and when MAP was lowered 61% with adenosine, CBF decreased only 28%. During hypotension, there was a marked reduction in cerebral vascular resistance. This was almost certainly on the basis of autoregulation rather than a direct effect of the adenosine since, as mentioned previously, adenosine has little effect on the cerebral circulation of dogs when it is delivered by the intravascular route.24 The reduction in CBF was inhomogeneous with respect to the various regions of the brain. The cerebral cortex and corpus callosum were most affected, while the brain stem was least affected. Previous studies have documented the varying completeness of autoregulation in different structures of the brain.37 The mechanisms and implications of these observations are unknown.

Adenosine has a number of properties which suggest that it may be useful for inducing systemic arterial hypotension. In contrast to nitroprusside, nitroglycerin, trimethaphan, and halothane, adenosine is a naturally occurring substance. In the doses employed in this study, adenosine appears to be nontoxic. In a

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**TABLE 4**

Regional changes in cerebral blood flow (ml/100 gm·min)*

<table>
<thead>
<tr>
<th>Blood Flow Region</th>
<th>Control Values</th>
<th>Dipyridamole Hypotensive Period</th>
<th>Recovery Period</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>30 Min</td>
<td>60 Min</td>
</tr>
<tr>
<td>cerebral cortex</td>
<td>97 ± 9</td>
<td>110 ± 12</td>
<td>63 ± 6†</td>
</tr>
<tr>
<td>cerebral hemispheres</td>
<td>70 ± 7</td>
<td>74 ± 8</td>
<td>46 ± 7†</td>
</tr>
<tr>
<td>corpus callosum</td>
<td>29 ± 3</td>
<td>28 ± 7</td>
<td>16 ± 3†</td>
</tr>
<tr>
<td>caudate nuclei</td>
<td>112 ± 13</td>
<td>114 ± 27</td>
<td>79 ± 14</td>
</tr>
<tr>
<td>brain stem</td>
<td>48 ± 5</td>
<td>51 ± 4</td>
<td>45 ± 7</td>
</tr>
<tr>
<td>cerebellum</td>
<td>60 ± 5</td>
<td>64 ± 8</td>
<td>41 ± 4†</td>
</tr>
<tr>
<td>total brain</td>
<td>65 ± 6</td>
<td>71 ± 8</td>
<td>46 ± 6†</td>
</tr>
</tbody>
</table>

* For an explanation of the three time periods, see text. Values are mean ± standard error of the mean. Significance: † = p ≤ 0.05; ‡ = p ≤ 0.01; § = p ≤ 0.001.

**TABLE 5**

Changes in arterial blood gases, hematocrit, and temperature*

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Control Values</th>
<th>Dipyridamole Hypotensive Period</th>
<th>Recovery Period</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>30 Min</td>
<td>60 Min</td>
</tr>
<tr>
<td>pH</td>
<td>7.33 ± 0.01</td>
<td>7.32 ± 0.02</td>
<td>7.27 ± 0.02†</td>
</tr>
<tr>
<td>PaCO₂ (mm Hg)</td>
<td>39.6 ± 0.4</td>
<td>37.6 ± 0.8</td>
<td>39.2 ± 0.2</td>
</tr>
<tr>
<td>PaO₂ (mm Hg)</td>
<td>172 ± 6</td>
<td>183 ± 9</td>
<td>170 ± 7</td>
</tr>
<tr>
<td>HCO₃⁻ (mEq/liter)</td>
<td>17 ± 1</td>
<td>16 ± 2</td>
<td>14 ± 1‡</td>
</tr>
<tr>
<td>hematocrit (%)</td>
<td>47 ± 3</td>
<td>43 ± 4</td>
<td>45 ± 2</td>
</tr>
<tr>
<td>temperature (°C)</td>
<td>37.2 ± 0.2</td>
<td>37.4 ± 0.1</td>
<td>37.3 ± 0.2</td>
</tr>
</tbody>
</table>

* For an explanation of the three time periods, see text. Values are mean ± standard error of the mean. Significance: † = p ≤ 0.05; ‡ = p ≤ 0.01; § = p ≤ 0.001.
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separate study in our laboratory, 1 hour of adenosine-induced hypotension to an MAP of 40 mm Hg had no adverse effect on neurological, hematological, or biochemical parameters in dogs. Adenosine is very rapidly inactivated in the circulation; hence the hypotension associated with its infusion is easily controlled and readily reversible. There is no tachyphylaxis during its administration and no rebound of arterial pressure above control levels following abrupt discontinuation. When administered by the intravenous route, adenosine probably does not dilate cerebral vessels or alter autoregulation. The fact that adenosine is not a primary cerebral vasodilator may be a distinct advantage in the neurosurgical environment. The degree of cerebral vasodilation associated with adenosine hypotension in this study is more or less in proportion to that required to sustain an adequate level of blood flow to the brain.

In summary, from a hemodynamic and pharmacological point of view, intravenous adenosine appears to have a variety of properties suggesting that it may be an effective clinical agent for inducing systemic arterial hypotension.

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