Paraplegia Following Thoracic Aortic Cross-Clamping in Dogs
No Difference in Neurological Outcome With a Barbiturate Versus Isoflurane

W.A.C. Mutch, MD; M.R. Graham, MD; W.C. Halliday, MD; J.M. Teskey, MD; I.R. Thomson, MD

Background and Purpose: We compared the incidence and severity of paraplegia following thoracic aortic cross-clamping in dogs for two anesthetic regimens. Animals were randomly assigned to receive methohexital (group M; n=9) or isoflurane (group I; n=9). We expected a better neurological outcome in animals administered methohexital because of superior neuronal protection and greater spinal cord perfusion pressure (mean arterial pressure below the cross-clamp site minus mean cerebrospinal fluid pressure).

Methods: After surgical preparation and a 30-minute stabilization period, dogs in group M received 14±6 mg·kg⁻¹·h⁻¹ methohexital to induce an isoelectric electroencephalogram followed by a continuous infusion of methohexital at 20 mg·kg⁻¹·h⁻¹. Dogs in group I received 1.4±0.2% end-tidal isoflurane (1 minimum alveolar concentration). The thoracic aorta was then occluded 2.5 cm distal to the left subclavian artery for 30 minutes and then released. Hemodynamics and cerebrospinal fluid pressure were measured at (1) baseline, (2) 2 minutes after aortic cross-clamping, (3) 20 minutes after aortic cross-clamping, (4) 5 minutes after aortic unclamping, and (5) 30 minutes after resuscitation. At 24 hours a neurological assessment was performed. After the clinical assessment the dogs were killed and the spinal cord removed immediately for histopathologic study.

Results: There were no differences in nasopharyngeal temperature, PaCO₂, pH, or hemoglobin at any time between groups. With cross-clamping, the spinal cord perfusion pressure decreased precipitously. However, there was no difference in spinal cord perfusion pressure between groups at any time (P=.5555). The neurological outcome, assessed at 24 hours after thoracic aortic cross-clamping by a veterinarian unaware of the anesthetic protocol, was not different between groups (P>.5, two-tailed Mann-Whitney rank-sums test). When anesthetized with methohexital 5 of 9 dogs were paraplegic; with isoflurane 7 of 9 dogs were paraplegic. By Spearman’s rank test, a strong inverse correlation between the Tarlov score and the ratio of dead to total lumbar anterior spinal cord neurons was seen (Spearman’s correlation coefficient = -0.8358; P=.0001).

Conclusions: We conclude that no advantage was offered by the choice of anesthesia to neurological outcome after 30 minutes of thoracic aortic cross-clamping in this canine model. (Stroke. 1993;24:1554-1560.)

Key Words: anesthesia • paraplegia • spinal cord • dogs

Paraplegia is a dreaded complication of surgical reconstruction of the thoracic aorta. The influence of the anesthetic on neurological outcome after cross-clamping of the thoracic aorta has not been well examined, however. Although a canine model of paraplegia after thoracic aortic cross-clamping has been widely used in laboratory investigations with various anesthetic techniques, there has been little attempt to standardize either the anesthesia protocols or the duration of cross-clamping. This makes direct compari-

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tion 24 hours after the proximal descending thoracic aorta had been clamped for 30 minutes, and histopathologically by microscopic examination of the lumbar spinal cord.

Materials and Methods
This study was approved by the Committee for Animal Experimentation at the University of Minnesota. Eighteen mongrel dogs (mean±SD weight, 20±2 kg) were randomly assigned to one of two groups depending on the anesthetic used: (1) methohexital, group M (n=9) or (2) isoflurane, group I (n=9).

Preparation
After induction of anesthesia with 25 mg·kg⁻¹ IV thiopental, the trachea was intubated and mechanical ventilation instituted. Anesthesia was maintained with isoflurane in oxygen, 1.4% end-tidal, and the Pao₂ was adjusted to 35 to 40 mm Hg. The dogs were placed in a modified sphinx position with the head fixed in a stereotaxic frame. A nasopharyngeal temperature probe was inserted, and body temperature was maintained at 37±1°C by a servo-controlled heating lamp and pad. Bipolar EEG electrodes were placed over the parietal hemispheres bilaterally. The EEG was continuously recorded by an Interspec Medical Neurotrac EEG monitor. Through the right femoral vein, a flow-directed catheter was advanced to the right ventricle and withdrawn slightly into the right atrium. A right femoral arterial catheter was advanced into the distal aorta. A 7.5F double-lumen catheter was inserted in the left internal mammary artery and advanced to the proximal aorta. Using a micromanipulator, a 22-gauge spinal needle was inserted in the cisterna magna to measure CSFP. The proximal descending aorta was exposed through a left thoracotomy.

Experimental Protocol
At least 30 minutes elapsed between completion of preparatory invasive procedures and the start of the experiment. With completion of surgery isoflurane was discontinued in group M and methohexital administered as a bolus to achieve an isoelectric EEG and a mean arterial pressure (MAP) of 90 mm Hg and then continuously infused at 20 mg·kg⁻¹·h⁻¹ to maintain EEG isoelectricity. In group I the end-tidal concentration of isoflurane was altered to yield an MAP of 90 mm Hg. Measurements of hemodynamics and CSFP were then made (baseline). The aorta was cross-clamped 2.5 cm distal to the left subclavian artery, and 2 minutes later all measurements were repeated (Clamp On 2 min). At 20 minutes all measurements were again repeated (Clamp On 20 min). The aortic cross-clamp was left in place for 30 minutes. Five minutes after unclamping, all measurements were repeated (Clamp Off). No attempt was made to control MAPproximal or Paco₂ immediately after unclamping. The animals were then resuscitated by blood volume expansion with crystalloid. In group M the methohexital infusion was continued if MAP was greater than 90 mm Hg or discontinued if less than this. Ventilation was adjusted to restore Paco₂ to baseline, and NaHCO₃ was administered if the base deficit exceeded 10 mmol·L⁻¹. A final set of measurements was made 30 minutes after complete resuscitation (stable MAP, central venous pressure [CVP], and acid-base status) (Resuscitation). All wounds were then sutured and infiltrated with 0.5% bupivacaine. Isoflurane was discontinued in group I, methohexital was discontinued, if still being infused, in group M, and the trachea was extubated. Oxygen was administered by face cone at 5 L·min⁻¹, and lactated Ringer’s solution was infused at 100 mL·h⁻¹ until the next day. Buprenorphine (0.015 mg·kg⁻¹ IM) was administered for analgesia and, if necessary, repeated the next morning. Exactly 24 hours after application of the aortic cross-clamp, neurological assessment was performed by a veterinarian who was unaware of the treatment group to which the animals belonged. She assessed the severity of paraplegia in each dog, using the Tarlov score: grade 0, no voluntary movement, spastic or flaccid paraplegia; grade 1, perceptible movement of joints; grade 2, good movement of the joints but unable to stand; grade 3, ability to stand and walk; grade 4, complete recovery. The animals were then killed by Euthanyl injection.

Data Acquisition
At each of the five measurement periods (Control, Clamp On 2 min, Clamp On 20 min, Clamp Off, and Resuscitation) we recorded temperature, MAPproximal, MAPdistal, CVP, and CSFP. Arterial blood gases and hemoglobin were determined before each measurement period using an ABL 3 acid-base laboratory (Radiometer). Pressures were measured by calibrated Gould P23 transducers positioned either at the level of the cisterna magna or, for the CVP transducer, at the right atrial level. SCPP was calculated as MAPdistal minus mean CSFP or CVP, whichever outflow pressure was greater. Data were recorded continuously on paper by a polygraph (Gould recorder 2600S) and intermittently on hard disk by a Gateway 2000 386 computer-based digital acquisition system (Dataq Instruments). Data presented are from the digital acquisition system.

Light Microscopy
In 14 of 18 experiments, after injection of Euthanyl the spinal cord was immediately removed and placed in 10% buffered formalin. After fixation, six representative cross-sectional tissue samples were obtained from the lumbar spinal cord and embedded in paraffin. Glass slides having 7-μm-thick sections were stained with hematoxylin and eosin. An observer unaware of the dog’s neurological outcome and anesthetic protocol examined each slide by light microscopy to count the total number of neurons in the anterior spinal cord (anterior to a line drawn through the central canal perpendicular to the vertical axis). These cells were considered dead if the cytoplasm was diffusely eosinophilic and viable if the cells demonstrated basophilic stippling (that is, contained Nissl substance). The ratio of dead to total lumbar anterior spinal cord neurons was calculated.

Data Analysis
Data were evaluated by analysis of variance (ANOVA) for repeated measures. The time effect on the possible differences between the two groups was tested by group×time interaction. When ANOVA revealed either a significant group×time interaction or time effect, appropriate multiple comparisons were made by the least-
TABLE 1. End-tidal Isoflurane Concentration in a Canine Model of Thoracic Aortic Cross-Clamping

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Clamp On 2 Min</th>
<th>Clamp On 20 Min</th>
<th>Clamp Off</th>
<th>Resuscitation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methohexital</td>
<td>0.08±0.04</td>
<td>0.08±0.06</td>
<td>0.06±0.04</td>
<td>0.08±0.05</td>
<td>0.19±0.20</td>
</tr>
<tr>
<td>(n=9)</td>
<td>(n=8)</td>
<td>(n=7)</td>
<td>(n=8)</td>
<td>(n=8)</td>
<td></td>
</tr>
<tr>
<td>Isoflurane</td>
<td>1.40±0.20</td>
<td>1.43±0.18</td>
<td>1.38±0.12</td>
<td>1.36±0.17</td>
<td>1.38±0.19</td>
</tr>
<tr>
<td>(n=9)</td>
<td></td>
<td>(n=8)</td>
<td>(n=8)</td>
<td>(n=7)</td>
<td></td>
</tr>
</tbody>
</table>

Values are mean±SD, expressed as percentage. See “Materials and Methods” for explanation of experimental protocol.

Results

In group M, animals received 14±6 mg·kg⁻¹ methohexital by bolus to induce an isoelectric EEG followed by a continuous infusion at 20 mg·kg⁻¹·h⁻¹. Total dose of methohexital administered was 34±19 mg·kg⁻¹. In group I animals, the end-tidal isoflurane was 1.4±0.2% before application of the thoracic aortic cross-clamp. The end-tidal concentrations of isoflurane in the two groups are shown in Table 1. For group M the end-tidal concentration was less than 0.1 minimum alveolar concentration (MAC) for the first four measurement periods. After resuscitation two animals received increased inspired isoflurane to control blood pressure (0.44% and 0.58% end-tidal isoflurane). In group I the end-tidal isoflurane concentration was stable at approximately 1 MAC end-tidal (1.4%).

Temperature and blood gas data for the two experimental groups are shown in Table 2. There were no group×time interactions for temperature, PaCO₂, pH, or hemoglobin. Immediately after unclamping, PaCO₂ was significantly higher than baseline values in both groups. The arterial pH decreased with cross-clamp release in both groups compared with baseline values, but there were no intergroup differences. The pH was restored to baseline values in both groups after the period of resuscitation. In only one animal was NaHCO₃ administered (10 mEq).

The pressure data for the two groups are shown in Table 3. Aortic cross-clamping caused a sharp increase in MAPproximal and decrease in MAPdistal in both groups. For MAPdistal there was a significant group×time interaction (P=.0440). However, there were no intergroup differences at any of the five measurement periods, as assessed by the least-squares means test with Bonferroni’s correction. With cross-clamping, the SCPP decreased precipitously in both groups. Five minutes after cross-clamp release SCPP had returned to baseline values in both groups. The groups did not differ significantly with respect to SCPP at any time period (P=.5555).

Neurological outcome was not different between groups (P>.5, two-tailed Mann-Whitney rank-sums test; Table 4). In group M, 5 of 9 animals were paraplegic; in group I, 7 of 9 animals were paraplegic.

There was a very strong inverse correlation of the Tarlov score versus the calculated ratio of dead to total lumbar anterior spinal cord neurons in 14 animals (Spearman’s correlation coefficient=−.8358; P=.0001; Figure). Comparison of the ratio of dead to total lumbar anterior spinal cord neurons did not differ between the two groups as assessed by unpaired t test (P=.4684).

TABLE 2. Temperature and Blood Gas Data in a Canine Model of Thoracic Aortic Cross-Clamping

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>Clamp On 2 Min</th>
<th>Clamp On 20 Min</th>
<th>Clamp Off</th>
<th>Resuscitation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temperature, °C</td>
<td>Methohexital</td>
<td>36.7±0.4</td>
<td>36.5±0.4</td>
<td>36.5±0.4</td>
<td>36.6±0.5</td>
</tr>
<tr>
<td></td>
<td>Isoflurane</td>
<td>36.8±0.6</td>
<td>36.5±0.4</td>
<td>36.5±0.3</td>
<td>36.4±0.3</td>
</tr>
<tr>
<td>PaCO₂, mm Hg</td>
<td>Methohexital</td>
<td>37.8±2.2</td>
<td>36.6±2.4</td>
<td>37.3±2.3</td>
<td>42.3±2.9*</td>
</tr>
<tr>
<td></td>
<td>Isoflurane</td>
<td>37.4±1.4</td>
<td>36.6±1.9</td>
<td>38.1±1.3</td>
<td>41.4±3.4*</td>
</tr>
<tr>
<td>pH</td>
<td>Methohexital</td>
<td>7.35±0.02</td>
<td>7.36±0.02</td>
<td>7.33±0.01</td>
<td>7.29±0.04*</td>
</tr>
<tr>
<td></td>
<td>Isoflurane</td>
<td>7.35±0.03</td>
<td>7.36±0.03</td>
<td>7.33±0.02</td>
<td>7.28±0.02*</td>
</tr>
<tr>
<td>Hemoglobin, g/dL</td>
<td>Methohexital</td>
<td>12.1±1.6</td>
<td>12.1±1.5</td>
<td>13.4±1.7</td>
<td>14.7±1.9*</td>
</tr>
<tr>
<td></td>
<td>Isoflurane</td>
<td>12.0±1.9</td>
<td>12.1±1.8</td>
<td>14.0±1.1</td>
<td>14.1±1.5*</td>
</tr>
</tbody>
</table>

Values are mean±SD; methohexital, n=9; isoflurane, n=9. See “Materials and Methods” for explanation of experimental protocol.

*P<.05 vs baseline within groups.
TABLE 3. Hemodynamic Data in a Canine Model of Thoracic Aortic Cross-Clamping

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline</th>
<th>Clamp On 2 Min</th>
<th>Clamp On 20 Min</th>
<th>Clamp Off</th>
<th>Resuscitation</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAP_{proximal}, mm Hg</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methohexital</td>
<td>84±8</td>
<td>121±11*</td>
<td>146±12*</td>
<td>87±15</td>
<td>95±14</td>
</tr>
<tr>
<td>Isoflurane</td>
<td>94±12</td>
<td>135±18*</td>
<td>162±25*</td>
<td>97±10</td>
<td>87±11</td>
</tr>
<tr>
<td>MAP_{distal}, mm Hg</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methohexital</td>
<td>86±7</td>
<td>12±4*</td>
<td>16±4*</td>
<td>91±19</td>
<td>98±15</td>
</tr>
<tr>
<td>Isoflurane</td>
<td>95±12</td>
<td>14±3*</td>
<td>14±3*</td>
<td>98±12</td>
<td>87±13</td>
</tr>
<tr>
<td>CVP, mm Hg</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methohexital</td>
<td>7.0±2.3</td>
<td>9.8±2.5*</td>
<td>9.4±1.9*</td>
<td>6.7±2.8</td>
<td>7.3±2.5</td>
</tr>
<tr>
<td>Isoflurane</td>
<td>6.7±2.5</td>
<td>9.3±2.3*</td>
<td>8.6±3.0*</td>
<td>5.9±2.6</td>
<td>6.1±2.7</td>
</tr>
<tr>
<td>CSFP, mm Hg</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methohexital</td>
<td>9.2±3.3†</td>
<td>12.1±3.7†</td>
<td>13.3±3.2*</td>
<td>11.8±3.7†</td>
<td>8.6±4.4</td>
</tr>
<tr>
<td>Isoflurane</td>
<td>12.8±3.0</td>
<td>15.6±3.5</td>
<td>14.5±3.8</td>
<td>17.0±7.0*</td>
<td>9.7±3.4*</td>
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<tr>
<td>SCPP, mm Hg</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methohexital</td>
<td>76±7</td>
<td>−1±4*</td>
<td>3±4*</td>
<td>79±20</td>
<td>88±15</td>
</tr>
<tr>
<td>Isoflurane</td>
<td>82±11</td>
<td>−3±4*</td>
<td>0±4*</td>
<td>81±17</td>
<td>76±14</td>
</tr>
</tbody>
</table>

Values are mean±SD; methohexital, n=9; isoflurane, n=9. MAP indicates mean arterial pressure; CVP, central venous pressure; CSFP, cerebrospinal fluid pressure; and SCPP, spinal cord perfusion pressure. See "Materials and Methods" for description of experimental protocol.

*P<.05 vs baseline within groups.
†P<.05 between groups.

Discussion

Our results demonstrate that the choice of anesthetic (methohexital or isoflurane) did not influence the severity of neurological outcome after thoracic aortic cross-clamping in dogs. These results contrast with other studies in the animal literature. Nylander et al. demonstrated that barbiturates modify the incidence of ischemic spinal cord injury before permanent infrarenal aortic occlusion in the dog. The incidence of paraplegia was 30% after barbiturates compared with 90% when halothane and nitrous oxide were used. It remains unclear, however, how administration of barbiturates could confer protection in the face of a permanent lesion. The same group has demonstrated similar results in a rabbit model when the infrarenal aorta was occluded for 25 minutes. Again in the rabbit, Naslund et al. have demonstrated that animals administered thiopental had a lower incidence of acute paraplegia than that seen in awake animals when both groups were subjected to 21 minutes of infrarenal cross-clamping. A benefit was not demonstrated between control animals and those administered halothane. No difference between thiopental and halothane was evident, however, if the acute- and delayed-onset paraplegia outcomes were combined. This is clearly the outcome of importance. Hypothermia provided complete protection irrespective of the anesthetic but when normothermic, 11 of 12 animals administered thiopental and 8 of 8 animals administered halothane were eventually paralyzed. Thus, a true protective effect of thiopental is not in evidence.

There is no consensus in the literature as to whether barbiturates are clearly superior to isoflurane for cerebral protection. Work from Nehls et al. suggests that neurological outcome is improved after middle cerebral artery occlusion for 6 hours when thiopental is administered to an isoelectric EEG compared with isoflurane to a similar anesthetic depth (P=.055). In contrast, Milde et al. saw no difference in

TABLE 4. Neurological Outcome at 24 Hours

<table>
<thead>
<tr>
<th>Tarlov Score</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methohexital</td>
<td>3</td>
<td>2</td>
<td>0</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Isoflurane</td>
<td>4</td>
<td>3</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>

Methohexital vs isoflurane, P>.5, two-tailed test (Mann-Whitney rank-sums test).

Plot shows Tarlov score vs ratio of dead to total lumbar anterior spinal cord neurons. There was a strong negative correlation between the Tarlov score and the dead to total neuron ratio (Spearman's correlation coefficient = −.8358; P=.0001) for pooled data. See text for methodology.
outcome after middle cerebral artery occlusion for 5 hours in monkeys administered either deep isoflurane or thiopental anesthesia. Both of these studies had problems, however. In the first study blood pressure was not similar during the ischemic period between groups despite vasopressor support of the blood pressure in the isoflurane group and vasodilator administration to the thiopental group. In the latter study, there was a 47% death rate, indicating a very severe ischemic insult. Baughman et al. demonstrated that deep isoflurane (2 MAC) was associated with improved neurological outcome after incomplete ischemia in rats compared with methohexital. Warner et al. demonstrated a decreased infarct volume in rats administered methohexital compared with isoflurane (both to EEG burst suppression). However, there was no difference in neurological outcome despite the difference in infarct volume.

In this study methohexital was administered in doses that resulted in an isoelectric EEG. Under such conditions the metabolic requirements of the neurons in the brain and, by inference, the neurons in the spinal cord are maximally depressed. Under such conditions neuronal protection is presumed to be maximal. We believe that there are three possible explanations for our failure to demonstrate improved outcome with methohexital administered to an end point of EEG burst suppression. First, there was no significant difference in SCPP between the groups at any time period. This was the case despite a significantly greater CSFP at baseline, after 2 minutes of cross-clamping, and after cross-clamp release in group I. These differences, although statistically significant, were not of large magnitude (3.5 to 5.2 mm Hg). Thus, the greater CSFP that was hypothesized with the volatile agent did occur, but the differences between groups were of a small enough magnitude that SCPP did not differ between groups. Oka and Miyamoto have shown that neurological outcome is dependent on the distal perfusion pressure after thoracic aortic cross-clamping in the dog. The importance of SCPP has recently been reemphasized in the work by Aadahl et al. These workers showed that spinal cord blood flow (SCBF), as assessed by the laser Doppler technique, is critically CSPP dependent. In a swine model, spinal cord pulsatile flux increased 51% with removal of 1 mL of cerebrospinal fluid. In our study, there was no difference in SCPP during cross-clamping, and these pressures were very low (maximum mean pressure, 3 mm Hg). These pressures are lower than those Oka and Miyamoto found to be associated with a moderate improvement of neurological dysfunction when the SCPP was increased from 0 to 7.5 mm Hg. Significant improvement was only seen if the SCPP was increased to 15 mm Hg in their canine model. In addition, we have shown that the lumbar spinal cord blood flow (SCBFlumbar) is very low (0.024±0.023 mL·g⁻¹·min⁻¹; n=21) with cross-clamping in barbiturate-anesthetized dogs with similar SCPP. This is not statistically different from a SCBFlumbar of 0.048±0.062 mL·g⁻¹·min (n=27; P=0.970, unpaired t test) seen with isoflurane anesthesia in another study from this laboratory. A trend to significant difference is present, however, and may have been manifest if the coefficient of variation for SCBFlumbar, in both groups, had not been so great. Even with documented higher regional cerebral blood flow with isoflurane, Warner et al. have demonstrated that ischemic thresholds for cerebral infarction are different for methohexital and isoflurane, with infarction occurring at greater regional cerebral blood flow with the volatile agent. Second, there is growing evidence that cerebral protection with an anesthetic agent may not relate exclusively to neuronal metabolic depression. Thus, the presumed advantage of maximal metabolic suppression with methohexital compared to that seen with 1 MAC end-tidal isoflurane may not exist.

Third, the hemodynamics of cross-clamp release were identical in the two groups of animals. We controlled for declamping shock within a 5-minute time frame, and there was no difference between the two groups in arterial blood pressure, heart rate, and cardiac output. We have previously demonstrated that blood pressure control may be important after declamping using a protocol similar to this study. We noted significantly better outcome in animals given methohexital compared with those anesthetized with isoflurane. However, hemodynamics after declamping were not as tightly controlled. In animals administered a higher end-tidal concentration of isoflurane (1.6±0.3%), there was significant declamping shock compared with animals administered methohexital. This is the most likely explanation for the discrepancy between those findings and those seen in this study. With tight hemodynamic control no difference in outcome is apparent. Crawford's group has shown, in humans, that the incidence of paraplegia after surgical reconstruction of the thoracic aorta or thoracoabdominal aorta was strongly correlated to perioperative hypotension. Additional periods of insult after an initial ischemic episode can result in markedly worsened neurological outcome in animal models.

It is possible that improved outcome might have been demonstrated if we had chosen thiopental as our barbiturate anesthetic. We chose methohexital instead of thiopental because a pilot study indicated that the dogs could not be easily aroused 48 hours after doses of thiopental, which ensured an isoelectric EEG before and during the 30-minute period of cross-clamping.

We found that 5 (56%) of 9 animals administered methohexital had paraplegia. In the isoflurane group 7 (78%) of 9 had paraplegia. A power analysis of these data (80% probability to detect this difference) indicates that 71 animals per group would be necessary to demonstrate a significant difference between groups at the 0.05% level. This finding alone indicates that if barbiturates are superior the effect is subtle. The strong negative correlation between the Tarlov score and the ratio of dead to total lumbar anterior spinal cord neurons, by Spearman's rank test, indicates that the "clinical" assessment of severity of paraplegia accurately predicts neurohistology.

In conclusion, we have shown that the incidence of paraplegia is not different when dogs were anesthetized with methohexital to an isoelectric EEG or when anesthetized with isoflurane after thoracic aortic cross-clamping of 30-minute duration. Confounding variables that could affect outcome were well controlled including temperature, hemodynamics, acid-base status, and hemoglobin. This study was designed to maximize the potential neural protective effects afforded by barbiturates (methohexital administered to an isoelectric EEG). Failure to demonstrate an advantage of barbiturates over isoflurane in this context suggests that the maximal metabolic depression that can be expected with
a barbiturate does not confer any additional advantage for spinal cord protection in this canine model.

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References


Editorial Comment

Animal models are often handicapped by the necessity for anesthesia. Findings obtained under the condition of anesthesia, ie, usually a drug-induced state that eliminates sensitivity to pain and sensory inputs, may not be extrapolatable to other situations. Central nervous system injury, for example, typically elicits a complex systemic and local tissue response including massive release of catecholamines, opioids, steroids, histamine, and other hormones or neurotransmitters. This injury response may contribute to secondary injury or may be neuroprotective. Anesthesia clearly dampens the injury response and thus should alter outcome. How anesthesia affects animal models is an important but unfortunately neglected question.

Mutch et al address this important question in the accompanying article. They compared neurological and histological outcomes in dogs anesthetized with methohexital or isoflurane and subjected to transient spinal cord ischemia by aortic cross-clamping. The results revealed a high correlation between histologically assessed motoneuronal ratios and a crude neurological outcome score, supporting the validity of the outcome measures chosen. The study found no significant differences in neurological or histological outcome in animals anesthetized by two anesthetic protocols.

Caution should be exercised when interpreting negative data. Most experimental hypotheses are designed
Paraplegia following thoracic aortic cross-clamping in dogs. No difference in neurological outcome with a barbiturate versus isoflurane.

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