The effect of blood transfusion, dopamine, and gamma hydroxybutyrate on posttraumatic ischemia of the spinal cord

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Posttraumatic spinal cord blood flow (SCBF) was assessed after elevating the mean systemic arterial pressure (mSAP) with a blood transfusion, or with an infusion of dopamine. The effect of the anesthetic agent, gamma hydroxybutyrate, was also assessed. Flows were measured using the $^{14}$C-antipyrine autoradiographic method. Animals were injured at T-1 by acute compression of the spinal cord with a clip exerting a pressure of 175 gm. Uninjured animals, with mSAP's of 120.0 ± 17.0 mm Hg, had gray and white matter flows of 74.2 ± 22.3 and 18.7 ± 6.7 ml/100 gm/min, respectively, while injured untreated animals had mSAP's of 82.5 ± 14.1 mm Hg and gray and white matter flows of 13.3 ± 12.1 and 3.9 ± 3.9 ml/100 gm/min, respectively, at the injury site. Blood transfusion raised the mSAP's to 127.5 ± 13.7 mm Hg in the injured animals and doubled the flows in gray and white matter to 25.6 ± 30.2 and 6.3 ± 6.4 ml/100 gm/min, respectively. Dopamine did not have as beneficial an effect as blood transfusion on either the mSAP (101.0 ± 16.7 mm Hg) or the SCBF (gray and white matter flows of 18.4 ± 12.4 and 5.8 ± 5.9 ml/100 gm/min). Gamma hydroxybutyrate (GHB) had almost no effect on the mSAP or SCBF of normal animals, and in injured animals produced only a unilateral increase in flow on the less severely injured side, without affecting the mSAP.

Key Words • spinal cord injury • blood flow • blood transfusion • dopamine • gamma hydroxybutyrate

Materials and Methods

Operative Procedure

Female white Wistar rats,* weighing 250 to 350 gm, were used. All animals were weighed and then anesthetized with pentobarbital (4 mg/100 gm intraperitoneally). Both femoral arteries and veins were cannulated with PE 50 polyethylene catheters containing a mixture of heparin and saline (10 IU heparin/ml saline). The right femoral artery cannula was connected to a Bell and Howell pressure transducer.† A

* Wistar rats obtained from Charles River Breeding Laboratories, Inc., Wilmington, Massachusetts.
† Pressure transducer, Model 4-327-010, manufactured by Bell and Howell, 360 Sierra Madre Villa, Pasadena, California.
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Hewlett Packard pressure amplifier coupled to a Hewlett Packard chart recorder provided continuous recording of the mSAP. The left femoral artery was used for intermittent sampling of arterial blood gases, and for sampling of the arterial tracer levels during the $^{14}$C-antipyrine infusion. The left femoral vein was used for infusion of the various agents used during the experiments, while the right femoral vein was used for infusion of the tracer and the KCl injection at the end of the tracer infusion.

Arterial blood gases were measured using the Radiometer blood gas system at 37°C. Blood gas values were corrected to the actual temperature of the animal. Animal temperature was monitored using a rectal probe and a radiometer, and temperature was maintained using a thermal blanket.

A tracheotomy was performed, and the animal was connected via a T-piece to a small-animal ventilator, adapted from a previous design. All animals were paralyzed with 1.2 mg pancuronium intravenously, and ventilated at a rate of 60 to 65 breaths/min with a tidal volume of 1 ml/100 gm, using a 2:1 mixture of nitrous oxide and oxygen.

After stabilization of the physiological parameters, all animals underwent laminectomy from C-7 to T-1. The animals in the trauma groups were injured at the T-1 level by acute extradural clip compression at a pressure of 175 gm for 1 minute, a method of injury developed in our laboratory as described previously. The clip was frequently checked to insure a consistent force of injury to all animals. All retractors were then removed, and the physiological parameters allowed to restabilize.

Experimental Protocol

As outlined in Table 1, there were six groups of animals in the experiment, four of injured animals, and two of uninjured animals. In one uninjured group, five animals served as an uninjured control group and had SCBF assessed approximately 30 minutes after completion of the laminectomy (see Table 1 for times of assessment of SCBF). The other uninjured group contained five animals which received 300 mg/kg GHB intravenously over 1 minute, beginning 15 minutes after completion of the laminectomy. The SCBF was then assessed at approximately 50 minutes after the laminectomy (35 minutes after the GHB infusion). Of the injured animals, one group of five animals received no treatment and served as injured controls. These animals had SCBF assessed approximately 30 minutes after injury. The next two groups received either a blood transfusion (six animals) or a dopamine infusion (five animals) beginning 15 minutes after injury as outlined below, and SCBF was assessed at about 35 minutes after injury. The last group of five animals had GHB (300 mg/kg) infused over 1 minute beginning 15 minutes after the injury, and SCBF was assessed 65 minutes after the injury.

Blood Transfusion

A red-cell suspension was prepared immediately prior to use from a donor Wistar rat which was anesthetized with pentobarbital (3 mg/100 gm intraperitoneally) and had one femoral artery and vein cannulated. The animal was given 290 IU/kg heparin intravenously, and then phlebotomized. A Sorvall GLC-1 centrifuge with an HL-4 rotor was used to spin the blood at 2514 G for 2 minutes. The red cells were then suspended in an equal volume of 0.9% saline and centrifuged again. This was repeated three times and the final suspension was used for infusion into the recipient animals. Two milliliters of the red cell suspension was infused over a 1-minute period beginning 15 minutes after injury, and then the infusion rate was adjusted with a Harvard pump to maintain an mSAP of 120 to 130 mm Hg for the duration of the experiment. The average volume transfused was 10.2 ± 5.1 ml/animal.

Dopamine Infusion

Dopamine HCl was diluted in 0.9% saline to a final concentration of 0.16 mg/ml. With the Harvard infusion pump, dopamine was infused at a rate sufficient to keep the mSAP between 100 and 120 mm Hg. The rate of infusion varied from 35 to 100μg/kg/min. With dopamine, a lower mSAP was the goal because it was not possible to consistently maintain the mSAP at values above 120 mm Hg.

Measurement of Spinal Cord Blood Flow

The $^{14}$C-antipyrine technique was used to assess SCBF, as previously described by Sandler and Tator and Rivlin and Tator. Each animal received

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‡ Pressure amplifier, Model 8805c, and chart recorder, Model 87758c, manufactured by Hewlett Packard/Medical Electronics Division, 175 Wyman Street, Waltham, Massachusetts.

§ Radiometer blood gas system, BMS Mk III, manufactured by Radiometer, Copenhagen, Denmark.

¶ Telethermometer, Model 425C, made by Yellow Springs Instrument Co., Inc., Yellow Springs, Ohio.

* Thermal blanket from Gorman-Rupp Industries, Belleview, Ohio.

† Ventilator built by Dr. W. Gentles at Sunnybrook Medical Centre, Toronto, Ontario, Canada, based on a design by Reale and Glaser.

‡ Gamma hydroxybutyrate obtained from Sigma Chemical Corp., St. Louis, Missouri.

§ Donor rat from Charles River Breeding Laboratories, Inc., Wilmington, Massachusetts.

¶ Sorvall GLC-1 centrifuge with an HL-4 rotor manufactured by Ivan Sorvall, Inc., Norwalk, Connecticut.

* Harvard pump, Model 2620, manufactured by Harvard Apparatus Co., Inc., 150 Dover Road, Millis, Massachusetts.

† Dopamine hydrochloride obtained from Desbergers Ltd., Montreal, Quebec, Canada.
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Fig. 1. Representative autoradiographs from uninjured controls, injured controls, and injured animals treated with blood transfusion, dopamine, or gamma hydroxybutyrate (G.H.B.). For each group, autoradiographs are shown from the injured level at T-1 and from the cord 0.1 cm caudad or cephalad to the injury level. A: Uninjured control animal showing normal spinal cord blood flow (SCBF). B: After injury, the injured cord at T-1 had almost no flow. Flow was also markedly depressed in the caudad and cephalad areas. C: Blood transfusion improved SCBF at the injury level. The gray matter outline, particularly the dorsal horns, can be seen. D: Dopamine produced less improvement of SCBF at the injury level as compared with blood transfusion. Only the dorsal gray horns can be seen faintly at the injury level. E: With GHB, an increase in SCBF was seen on the right side of the cord at the injury level.

75 μCi/kg of tracer dissolved in 0.9% saline and infused over a 1-minute period by a Sage pump.‡ Arterial blood was sampled at the start of the tracer infusion and at 10-second intervals during the infusion. At the end of the 1-minute infusion, cardiac arrest was induced with intravenous KCl. A laminectomy of C-5, C-6, and T-2 and T-3 was then performed and the spinal cord removed and frozen in 2-methylbutane chilled in liquid nitrogen. Sections of cord 20-μm thick were cut in a cryostat and air dried, and autoradiographs were made as previously described. The sites examined included the injury site at T-1, areas 0.1 cm cephalad and caudad to the injury site and, in some animals, more distant areas as well. Representative autoradiographs of each of the groups are shown in Fig. 1.

Analysis

From each animal, at least one section was analyzed from the injury site and from areas 0.1 cm cephalad, and 0.1 cm caudad to it. A scanning microscope

‡ Sage pump, Model 351, made by Sage Instruments, Division of Orion Research, Inc., Cambridge, Massachusetts.
Posttraumatic spinal cord blood flow

### TABLE 1

<table>
<thead>
<tr>
<th>Physiological Parameters</th>
<th>No Injury Groups</th>
<th>Injury Groups</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>GHB</td>
</tr>
<tr>
<td>no. of animals</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>prelaminectomy mSAP (mm Hg)</td>
<td>159.0 ± 6.0</td>
<td>168.5 ± 10.0</td>
</tr>
<tr>
<td>pretreatment mSAP (mm Hg)</td>
<td>146.0 ± 13.9</td>
<td>132.0 ± 35.1</td>
</tr>
<tr>
<td>posttreatment (pre SCBF) mSAP (mm Hg)</td>
<td>37.6 ± 0.9</td>
<td>38.2 ± 0.9</td>
</tr>
<tr>
<td>temperature (°C)‡</td>
<td>37.3 ± 0.03</td>
<td>7.40 ± 0.03†</td>
</tr>
<tr>
<td>pO2 (mm Hg)§</td>
<td>45.9 ± 14.6</td>
<td>151.7 ± 8.7</td>
</tr>
<tr>
<td>pCO2 (mm Hg)§</td>
<td>40.3 ± 3.2</td>
<td>41.9 ± 4.2</td>
</tr>
<tr>
<td>time from injury to KCl (min)§</td>
<td>26 ± 6</td>
<td>50 ± 7</td>
</tr>
</tbody>
</table>

* All values are mean ± standard deviation. GHB = gamma hydroxybutyrate; mSAP = mean systemic arterial pressure; SCBF = spinal cord blood flow.

† Significantly different from respective controls (p < 0.05).
§ Values taken at most 5 minutes prior to SCBF assessment. Corrected to the animals' temperature.
w For uninjured animals, this was the time from completion of the laminectomy until assessment of SCBF.

Results

Table 1 gives the physiological parameters for each of the groups. The prelaminectomy mSAP, preinjury mSAP, and arterial blood gases were similar to values found by other investigators. There were no significant differences in the prelaminectomy mSAPs among the six groups. During the injury, the characteristic acute rise in mSAP to between 250 and 300 mm Hg occurred, followed within 1 to 2 minutes by profound hypotension with an mSAP of about 70 mm Hg. The injured control animals, and the GHB-treated injured animals had similarly low mSAPs of 82.5 and 77.0 mm Hg, respectively, and these were significantly lower than the mSAP of the uninjured control animals (120.0 mm Hg). Treatment with blood or dopamine resulted in a significant elevation of the mSAP (p < 0.05). Indeed, in the blood transfusion group the mSAP rose to 127.5 ± 13.7 mm Hg, a level not significantly different from the mSAP of the uninjured control group (120.0 ± 17.0 mm Hg).

There were no significant differences in pO2 or temperature among the groups at the time of SCBF measurement (Table 1). However, the uninjured control group had a pH of 7.33 ± 0.03, which was significantly lower than all the other groups, except the dopamine group. The pCO2 of 40.3 ± 3.2 mm Hg in the uninjured control group was not significantly different from the other groups except for the dopamine group. The explanation for this mild metabolic...
Acidosis in this control group is not clear. The effect on SCBF of this small difference in pH is unknown, but one would expect, if anything, a mild vasodilation with a resultant increase in flow.

Among the injured animals, the dopamine group had a significantly elevated pCO2 and a lower pH compared with the injured controls. Indeed, there was great difficulty in maintaining a normal pCO2 in this group during the infusion. The increased pCO2 would tend to increase the SCBF by 0.15 to 0.62 ml/100 gm/min/mm Hg.

The SCBF values in uninjured control and uninjured GHB-treated animals are shown in Table 2. Overall normal gray and white matter flows at T-1 were 74.2 ± 22.3 and 18.7 ± 6.7 ml/100 gm/min, respectively. Values at the levels 0.1 cm cephalad and 0.1 cm caudad to the injury site were slightly higher. Gray matter flows were 88.5 ± 32.5 and 82.7 ± 25.0 ml/100 gm/min at the 0.1 cm cephalad and 0.1 cm caudad levels, respectively, and white matter flows were 20.7 ± 7.7 and 19.1 ± 5.7 ml/100 gm/min at the 0.1 cm cephalad and 0.1 cm caudad levels, respectively. These values are similar to those previously reported from this laboratory, and in addition the gray to white matter flow ratios of approximately 4:1 are similar to those described previously.

As shown in Table 2, GHB had no effect on the SCBF in most areas of the cord in the uninjured animals. Only a minor elevation occurred in the dorsal column at the 0.1 cm cephalad level and in the left ventrolateral area at the 0.1 cm caudad level, and a minor decrease occurred in the gray matter flow at the 0.1 cm cephalad level. It is noteworthy that there was no effect at the T-1 level and no effect on overall white matter flow at any level.

Table 3 shows the regional SCBF for the four groups of injured animals. The injured control animals had overall gray and white matter flows of 13.3 ± 12.1 and 3.9 ± 3.9 ml/100 gm/min, respectively at the T-1 level. Thus, 30 minutes after the acute compression injury lasting 1 minute, the gray matter flow was 21% that of normal, and white matter flow 19% that of normal. The effects of trauma were still evident at the 0.1 cm cephalad and caudad levels, although not as marked. For example, at the 0.1 cm cephalad level, gray matter flow was 52% and white matter flow was 48% of normal, and, at the 0.1 cm caudad level, gray matter flow was 58% and white matter flow was 53% of normal. After trauma, the ratio of gray to white matter flow was still approximately 4:1.

Blood transfusion resulted in significantly increased SCBF in all white matter areas at the injury level, the dorsal columns, and the right and left ventrolateral column areas at the 0.1 cm caudad level, and the left ventrolateral column area at the 0.1 cm cephalad level (Table 3). Flows in other white matter areas also tended to be increased. Indeed, the overall white matter flows at the 0.1 cm caudad and cephalad levels were significantly greater than control flows. After blood transfusion, gray matter flows were also significantly increased at the injury level and 0.1 cm caudad levels. In general, flows in gray and white matter at the injury site nearly doubled, and the increases appeared to be proportional because the 4:1 gray to white matter flow ratio was well maintained. Although the increases were most noticeable at the injury level where flow doubled, flow at the caudad level increased 40% in the white matter and 30% in the gray matter. At the cephalad level, flow increased only 20% in the white matter and not at all in the gray. Although hemorrhages were seen in many animals, none of the hemorrhages were radioactive in the autoradiographs, indicating that bleeding had ceased prior to radioisotope infusion for the SCBF measurement.

Dopamine infusion resulted in an increase in flow primarily at the injury level, but these increases were not as marked as with the blood transfusion. In general, flow increased by about 50% at the injury level. At the other levels, the effects were variable, with some areas showing increased flow (the left ventrolateral column 0.1 cm caudad, and gray matter 0.1 cm cephalad) and some areas decreased flow (the dorsal column 0.1 cm cephalad and left dorsolateral column 0.1 cm caudad). The slightly elevated pCO2 would increase flows by 0.5 to 3.0 ml/100 gm/min, and thus flow increases with dopamine may in part be due to the elevated pCO2 rather than the increased mSAP alone. No radioactive hemorrhages were seen in this group.

Gamma hydroxybutyrate increased the flow slightly, but significantly, in the right dorsolateral and right ventrolateral columns and gray matter areas, both at the injury level and 0.1 cm caudad to the injury level. However, GHB had no effect on flow in the remaining areas at T-1 or 0.1 cm caudad, and had no effect on flow in any of the areas 0.1 cm cephalad to the injury site.

Discussion

Our laboratory has been exploring the hypothesis that elevation of the systemic blood pressure may improve neurological recovery after acute spinal cord injury, a hypothesis based on several known features of acute cord injury. For example, spinal cord injuries have been shown to produce severe cord ischemia. Several studies have shown that severe cord injury causes significant systemic hypotension. In addition, autoregulation in the cord is lost at the site of injury, as has been shown by Palleske and others. Also, Brodkey, et al., have shown that elevating the systemic blood pressure after the loss of cord conductivity due to cord compression resulted in a return of the evoked potential. Senter and Venes have also considered this therapeutic modality. With Aramine, they raised the mSAP to

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TABLE 2
Spinal cord blood flow in uninjured control and GHB-treated animals*

<table>
<thead>
<tr>
<th>Group</th>
<th>Spinal Cord Level</th>
<th>White Matter</th>
<th>Gray Matter</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>DC</td>
<td>RDL</td>
</tr>
<tr>
<td></td>
<td>control</td>
<td>(n = 65)</td>
<td>(n = 50)</td>
</tr>
<tr>
<td></td>
<td>(5)</td>
<td>20.4 ± 8.2</td>
<td>19.5 ± 9.7</td>
</tr>
<tr>
<td></td>
<td>GHB</td>
<td>(n = 50)</td>
<td>(n = 50)</td>
</tr>
<tr>
<td></td>
<td>(5)</td>
<td>22.7 ± 4.9</td>
<td>19.4 ± 6.4</td>
</tr>
<tr>
<td>0.1 cm caudad to T-1</td>
<td>control</td>
<td>(n = 50)</td>
<td>(n = 50)</td>
</tr>
<tr>
<td></td>
<td>(5)</td>
<td>24.0 ± 6.1</td>
<td>18.2 ± 4.2</td>
</tr>
<tr>
<td></td>
<td>GHB</td>
<td>(n = 50)</td>
<td>(n = 50)</td>
</tr>
<tr>
<td></td>
<td>(5)</td>
<td>23.3 ± 6.5</td>
<td>19.4 ± 5.5</td>
</tr>
<tr>
<td>0.1 cm cephalad to T-1</td>
<td>control</td>
<td>(n = 50)</td>
<td>(n = 50)</td>
</tr>
<tr>
<td></td>
<td>(5)</td>
<td>21.5 ± 6.2</td>
<td>20.3 ± 9.3</td>
</tr>
<tr>
<td></td>
<td>GHB</td>
<td>(n = 50)</td>
<td>(n = 50)</td>
</tr>
<tr>
<td></td>
<td>(5)</td>
<td>24.2 ± 5.6</td>
<td>18.4 ± 4.7</td>
</tr>
</tbody>
</table>

* Values are mean ± standard deviation (ml/100 gm/min), n = number of autoradiographic points averaged. GHB = gamma hydroxybutyrate. In the white matter: DC = dorsal columns; RDL = right dorsolateral columns; LDL = left dorsolateral columns; RVL = right ventrolateral columns; LVL = left ventrolateral columns (see Fig. 2).

† Significantly different from control values (p < 0.05).

TABLE 3
Spinal cord blood flow in injured control and treated animals*

<table>
<thead>
<tr>
<th>Group</th>
<th>Spinal Cord Level</th>
<th>White Matter</th>
<th>Gray Matter</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>DC</td>
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<tr>
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<td>control</td>
<td>(n = 110)</td>
<td>(n = 110)</td>
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<td></td>
<td>(6)</td>
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<td>(5)</td>
<td>7.2 ± 6.5</td>
<td>6.0 ± 6.1</td>
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<td></td>
<td>dopamine</td>
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<td>(n = 120)</td>
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<td></td>
<td>(5)</td>
<td>5.5 ± 6.0†</td>
<td>5.2 ± 6.1</td>
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<tr>
<td></td>
<td>GHB</td>
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<td>(n = 100)</td>
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<td>(5)</td>
<td>4.3 ± 1.2</td>
<td>5.0 ± 5.3†</td>
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<td>0.1 cm caudad to T-1</td>
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<td>(n = 40)</td>
<td>(n = 40)</td>
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<td></td>
<td>(5)</td>
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<td>12.2 ± 5.6</td>
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<tr>
<td></td>
<td>blood</td>
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<td>(n = 50)</td>
</tr>
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<td></td>
<td>(6)</td>
<td>14.0 ± 6.8†</td>
<td>13.6 ± 7.6</td>
</tr>
<tr>
<td></td>
<td>dopamine</td>
<td>(n = 50)</td>
<td>(n = 50)</td>
</tr>
<tr>
<td></td>
<td>(5)</td>
<td>9.2 ± 5.7</td>
<td>13.0 ± 5.8†</td>
</tr>
<tr>
<td>0.1 cm cephalad to T-1</td>
<td>control</td>
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<td>(n = 50)</td>
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<td>blood</td>
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<td>(n = 60)</td>
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<td></td>
<td>(6)</td>
<td>12.3 ± 9.7</td>
<td>14.0 ± 7.1†</td>
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<td></td>
<td>dopamine</td>
<td>(n = 50)</td>
<td>(n = 50)</td>
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<td>7.8 ± 5.2†</td>
<td>10.7 ± 5.0</td>
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<td></td>
<td>GHB</td>
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<td>(n = 50)</td>
</tr>
<tr>
<td></td>
<td>(5)</td>
<td>8.8 ± 6.7</td>
<td>9.5 ± 6.4</td>
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</table>

* Values are mean ± standard deviation (ml/100 gm/min). n = number of autoradiographic points averaged. In white matter: DC = dorsal columns; RDL = right dorsolateral columns; LDL = left dorsolateral columns; RVL = right ventrolateral columns; LVL = left ventrolateral columns (see Fig. 2).

† Significantly different from controls (p < 0.05).

normal levels in cats injured by the weight-dropping model, and produced a rise in the SCBF in white matter to either normal or hyperemic levels for the first few hours after injury. Senter, et al.,33 also showed that GHB, a central nervous system depressant, could raise the SCBF in both normal animals and animals injured by the weight-dropping technique.

In our laboratory, SCBF has been studied after acute cord compression injury in monkeys, using an inflatable cuff as the injury device,27,28 and in rats,
using a modified aneurysm clip. In these experiments, major cord injury produced severe ischemia which occurred immediately and persisted. For example, in monkeys, there was a drop in flow immediately after injury to less than 1 ml/100 gm/min, and this persisted for 24 hours after severe injury. Moderate trauma, however, resulted in gradually increasing flows beginning 1 hour after injury, with flows rising to even higher than normal values in the white matter at 24 hours. In the present experiments, we studied the effects of posttraumatic elevation of mSAP on the SCBF after an acute severe compression injury of 1 minute, with the clip exerting a pressure of 175 gm at T-1. This injury has been shown to result in major weakness of the hindlimbs, with only minimal recovery after 8 weeks as defined by the inclinoplane technique. In all of the present experiments, treatment began 15 minutes after injury.

The 14C-antipyrine autoradiographic technique relies on the Kety-Schmidt equation for the determination of the regional blood flow. One of the factors that must be known in order to use the equation is the 14C-antipyrine partition coefficient, that is, the ratio of the solubility of the tracer in the tissues as compared with its solubility in blood. The value initially derived for rat brain gray and white matter was 0.99, and this laboratory and others have used this value in the study of brain and spinal cord blood flow. This value has recently been revised by Sakurada, et al. to 0.91 for both gray and white matter. We have continued to use 0.99 for the partition coefficient, and thus our values are probably slightly higher than the true values. Recently, it has been shown that 14C-iodoantipyrine more accurately reflects blood flow at high flow values, but, in ischemic situations and for flows less than 50 ml/100 gm/min, the flow values are similar for both tracers.

The 14C-antipyrine technique can only sample SCBF at one time for each animal. In all injured animals except the GHB-treated group, SCBF was assessed 30 minutes after injury. Previous work has shown severe spinal cord ischemia at this time, and with autoregulation lost one would have expected to see an elevation of SCBF by this time. The SCBF in GHB-treated animals was assessed approximately 45 minutes after injection (60 minutes after injury), because at this time the peak depressant effect of GHB should have been evident, and the maximum effect on SCBF should have occurred. Uninjured animals had normal blood gases and mSAP, and the spinal cord gray and white matter flows at the T-1 level were 74.2 ± 22.3 and 18.7 ± 6.7 ml/100 gm/min, respectively. Flow at levels 0.1 cm caudad and cephalad to the injury site was higher and may reflect the slightly poorer vascular supply at the T-1 level.

Normal blood gases at the time of SCBF assessment were seen in all injured animals except for the dopamine group, in which the pCO2 was elevated (Table 1). The exact etiology of this increase is unknown, but it may be the result of constriction of airways, and decreased lung perfusion coupled with increased pooling of blood in the lungs. In this group, there was difficulty in keeping the pCO2 within normal limits.

The injured untreated animals were significantly hypotensive (p < 0.05), with an mSAP of 82.5 ± 14.1 mm Hg, and showed a decreased flow to about 20% of normal (gray and white matter flows at T-1 were 13.3 ± 12.1 and 3.9 ± 3.9 ml/100 gm/min, respectively). Flows were also significantly decreased in the areas 0.1 cm caudad and 0.1 cm cephalad to the injury site, but not as markedly depressed as in a previous study from this laboratory, in which a more severe injury was made with a 180-gm clip compressing the spinal cord for 5 minutes.

Red-cell infusion effectively reversed the postinjury hypotension, and raised the mSAP to normal levels (Table 1). Dopamine was not as effective as blood, and raised the mSAP to only 84% of normal. In the transfused animals, the rise in the mSAP to normal resulted in a doubling of the SCBF at the injury site, whereas dopamine only increased SCBF by 50%, probably reflecting the lower mSAP achieved in this group. The lack of radioactive hemorrhages seen after blood pressure elevation with these agents is worth noting (Fig. 1). Despite an increase in flow to the area, no blood leaked from the injured vessels.

Gamma hydroxybutyrate (GHB) has been shown to be a potent anesthetic agent, to have a protective effect against the development of brain edema, and to be beneficial to the hypoxic brain. In the dose used in the present experiments, GHB had no significant effect on the mSAP of control animals, and no effect was seen on the mSAP of the spinal cord-injured animals. Gamma hydroxybutyrate had no effect in the untreated animals on overall or regional SCBF at the T-1 level, and there were only minor changes at the other levels. In contrast, GHB given after injury produced specific changes in SCBF. Flows...
increased slightly but significantly in the gray matter at the T-1 and 0.1 cm caudal levels, but the white matter flow increased only on the right side of the spinal cord at the T-1 and 0.1 cm caudal levels. These findings may be related to a slightly increased severity of injury on the left side of the cord due to the clip being applied to the spinal cord with the tips of the blades pointing toward the animals’ right side (see Fig. 3 of Rivlin and Tato). Thus, the left side of the spinal cord was always nearer the fulcrum of the clip and would have received a slightly more severe compressive force than the right side. Accordingly, it was the less severely injured white matter on the right side of the spinal cord that showed an increased SCBF after GHB. No effect was seen with GHB at the 0.1 cm cephalad level.

The results of the present experiments with GHB differ markedly from those of Senter, et al., who were able to raise SCBF in normal animals and to counteract the posttraumatic ischemia in cats injured by the weight-dropping technique. The reasons for these differences are unknown, but certain points of difference in the experiments may be of importance. Senter, et al., used 300 mg/kg of GHB infused over a period of 15 minutes, and measured SCBF 1 hour after infusion. We used the same dose of 300 mg/kg, but infused it over 1 minute, and measured SCBF 45 minutes later. This latter method was used effectively by MacMillan in his studies on brain ischemia in rats. Thus, the mode of administration would not appear to account for the lack of effect of GHB in the present experiments. The fact that uninjured animals in our experiment showed no increase in SCBF after GHB injection may reflect a species difference between cats and rats. The observation that GHB increased flow on only the less severely injured side of the rat cord suggests that the severity of the spinal cord injury may play a role in the effectiveness of GHB. With the severe, sustained compression injury used in the present study, there is an immediate decrease in SCBF, in contrast with the delayed ischemia seen by Senter, et al., after a weight-dropping injury where the compression lasts only milliseconds.

The continuous compression for 1 minute in our model may produce a “no reflow” type of phenomenon. This may be due to an inability, even with elevation of the mSAP, to exceed the critical opening pressure of the cord vessels, particularly of the larger veins, which may be due to vasospasm or microvascular occlusion. As yet, there is no knowledge regarding the exact mechanism responsible for the decrease in SCBF seen with the clip compression model, and the role of the various factors just mentioned is speculative.

Further experiments using this and other models are therefore necessary to elucidate the differences between our results and those of Senter, et al., with regard to the basic pathophysiology of the different types of spinal cord injury and the differences in the effects of treatment. More work is needed to determine if restoration of systemic pressure to normal levels or even to hypertensive levels has any role in the management of acute spinal cord injury.

Acknowledgments

The authors are grateful to Mrs. L. Marmash, Mr. H. C. Lai, Mr. I. Kerr, and Mrs. T. Hupe for their invaluable technical assistance. We are indebted to Dr. W. Gentles for construction of the ventilator used.

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J. Neurosurg. / Volume 56 / March, 1982

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Manuscript received August 10, 1981.

Dr. Dolan was a Medical Research Council Fellow during the course of this study.

The study was supported by Medical Research Council of Canada Grant MT4047.

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