The Technique of Nitroprusside Administration Modifies the Intracranial Pressure Response

L. F. Marshall, M.D., ‡ H. M. Shapiro, M.D.§

Sodium nitroprusside (SNP) can increase intracranial pressure (ICP) in the presence of intracranial space-occupying lesions. The authors examined the influences of the technique of SNP administration on the ICP response in cats with intracranial hypertension (14.8 ± 1.2 torr) secondary to inflated epidural balloons. The rate of SNP infusion and the PaO₂ and PaCO₂ levels were varied. One group (I) received a slow drug infusion and the second (II) had a rapid SNP injection to effect a decrease in blood pressure (BP) of 60–70 torr. These major groups were further subdivided according to blood-gas status into a, normocarbic/normoxic, b, hypocarbic/hyperoxic, and c, hypocarbic/normoxic groups. BP, ICP, electroencephalogram (EEG) and end-tidal CO₂ were continuously recorded and arterial blood sampled intermittently for determination of blood-gas values. With a slow SNP infusion (Group I), ICP did not change significantly. When SNP was administered rapidly (Group II), ICP increased significantly above control values in all subgroups. Group Ila animals had the largest average ICP increase (18.6 ± 3.7 torr), which occurred at 2 min. In Group IIc, the ICP response peaked earliest (at 50 sec) and was significantly greater than that in Group Iib. EEG depression accompanied the ICP changes in Group II animals. When intracranial hypertension is present, SNP should be given slowly under conditions of hypocarbic and hyperoxic. (Key words: Anesthesia, neurosurgical. Anesthetic techniques: hypotension, induced, nitroprusside. Brain: intracranial pressure.)

In the presence of a space-occupying lesion, infusion of sodium nitroprusside (SNP) can lead to marked intracranial hypertension and neurologic changes.1–3 Because SNP is frequently used to control blood pressure in neurosurgical patients, we have defined the optimal circumstances for its administration in cats with intracranial mass lesions. To accomplish this, we examined the influences of modifying the rate of the SNP infusion and altering arterial blood-gas status on intracranial pressure (ICP).

Methods

Thirty-four cats weighing 2.5–4.0 kg were anesthetized with pentobarbital, 30 mg/kg, intraperitoneally.

* Assistant Professor of Anesthesiology.
† Research Associate in Anesthesiology.
‡ Assistant Professor of Neurosurgery.
§ Associate Professor of Anesthesiology/Neurosurgery.

Received from the Departments of Anesthesia and Surgery (Neurosurgery) Research Service, Veterans Administration Hospital, San Diego, University of California at San Diego, and George Washington University Medical Center, Washington, D. C. Accepted for publication May 14, 1979. Presented in part at Annual Meeting of the American Society of Anesthesiologists, October 1977.

Address reprint requests to Dr. Shapiro: Anesthesia Research, V-151, Veterans Administration Hospital, 3350 La Jolla Village Drive, San Diego, California 92161.
NITROPRUSSIDE AND ICP

**Fig. 1.** Comparison of intracranial pressure (ICP) and blood pressure (BP) effects of sodium nitroprusside administered slowly (a, left) and rapidly (b, right) in two cats. ↑ arrow indicates beginning and termination of infusion. Similar levels of hypotension are achieved by either infusion technique; however, ICP increases markedly with the rapid administration.

cats, breathed room air (P_{aO_2} 103 ± 5 torr) at normocarbia (P_{aCO_2} 33 ± 2 torr). Groups Ib and IIb, represented by five and seven cats, respectively, inspired 100 percent oxygen, and their lungs were hyperventilated (P_{aCO_2} 427 ± 13 torr, P_{aCO_2} 22 ± 2 torr). Last, Group IIc breathed room air during hyperventilation (P_{aCO_2} 103 ± 5 torr, P_{aCO_2} 22 ± 2 torr). All data were analyzed with the Student t test for unpaired data. Statistical significance is reported at P < 0.05 or less.

**Results**

The two major groups of animals were similar in the total doses of SNP needed to sustain the desired level of hypotension. These doses, 440 ± 25 μg/kg/min in Group I and 470 ± 30 μg/kg/min in Group II, though markedly greater than clinical requirements, were anticipated from previous laboratory trials.¶ In Group II, a rather high initial dose was necessary, but this could be tapered off during the 2-min trial. In contrast, Group I received modest early doses, which necessitated continuous modulation to offset blood pressure fluctuations during the 5-min SNP administration period.

During a slow SNP infusion, the decrease in blood pressure was gradual and sustained, while the increase in ICP was modest and protracted (∆ICP = 8 torr) (fig. 1). As ICP increased, the intracranial systolic-diastolic pulse pressure also increased. In Group II, as blood pressure was decreased ICP increased precipitously (fig. 1b; ∆ICP = 15 torr). Unlike the Group I animals, these cats experienced appreciable end-tidal CO₂ decreases and simultaneous EEG slowing with increasing voltage.

In Group I, the decreases in blood pressure were comparable for the two subgroups (normocarbic/normoxic and hypocarbic/hyperoxic). The changes in ICP were gradual, modest and random (fig. 2). As a result, the cerebral perfusion pressures (CPP = BP – ICP) were similar. In computing cerebral perfusion pressure, cerebral venous pressure was considered negligible, since the head was fixed well above heart level (<12.5 cm).

In contrast to Group I, ICP increased significantly from initial values in Group II, and blood-gas status modified the ICP response (fig. 3). Three subgroups are represented: a, normocarbic/normoxic, b hypocarbic/hyperoxic, and c, hypocarbic/normoxic cats. While absolute blood pressure responses to the rapid SNP infusion did not differ significantly among the

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**Table 1. Study Groups Based on SNP Infusion Rates and Arterial Blood-gas Status**

<table>
<thead>
<tr>
<th></th>
<th>Infusion Rate</th>
<th>P_{aO_2} (torr)</th>
<th>P_{aCO_2} (torr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group Ia</td>
<td>Slow</td>
<td>33 ± 2</td>
<td>108 ± 5</td>
</tr>
<tr>
<td>Group Ib</td>
<td>Slow</td>
<td>22 ± 2</td>
<td>427 ± 13</td>
</tr>
<tr>
<td>Group IIa</td>
<td>Rapid</td>
<td>33 ± 2</td>
<td>105 ± 5</td>
</tr>
<tr>
<td>Group IIb</td>
<td>Rapid</td>
<td>22 ± 2</td>
<td>427 ± 13</td>
</tr>
<tr>
<td>Group IIc</td>
<td>Rapid</td>
<td>22 ± 2</td>
<td>105 ± 5</td>
</tr>
</tbody>
</table>

* Slow infusion occurred over a 5-min period (X_{mean} = 440 ± 25 μg/kg/min); rapid infusion lasted 2 min (X_{mean} = 470 ± 30 μg/kg/min). Both rates achieved BP decreases of 60–70 torr from the control level. Means (±SEM) are indicated.
subgroups, Group IIa had a higher initial blood pressure. This group sustained the earliest and greatest ICP increases (18.6 ± 3.7 torr). The hypocarbic/hyperoxic cats, Group IIb, recorded the smallest ICP increases, which were significant at 4 min. Group IIC, the hypocarbic/normoxic animals, initially mimicked their normocarbic (Group IIa) counterparts (ΔICP > +8 torr), but thereafter developed ICP levels comparable to those of Group IIb. Because of the high initial BP among Group IIa, these animals sustained the highest cerebral perfusion pressure despite the significant concurrent increases in ICP.

Discussion

Our study indicates that the margin of safety for use of SNP in cats with intracranial hypertension can be improved by attention to the administration technique. We found that the SNP infusion rate and arterial blood-gas status are important considerations. In our experimental model for intracranial hypertension, we verified the persistence of cerebral vascular CO₂ reactivity by the inhalation of carbon dioxide. This maneuver also demonstrated a decrease of intracranial compliance due to inflation of the epidural balloon. Prior to SNP infusion, both normocarbic groups sustained higher initial blood pressure values. This may be related to the enhanced circulating catecholamine levels due to the arterial carbon dioxide tension.⁷

When SNP was infused slowly (Group I), providing constant blood pressure control, the ICP changes were random and insignificant. This blunted ICP response, compared with Group II, suggests a number of possibilities. First, the rapid SNP infusion may have caused cerebrovasodilatation that paralleled the systemic event. This quick response precluded spatial compensation. Second, autoregulation may have been selectively impaired, especially in Group IIa, such that the relatively higher systemic blood pressure was transmitted to the cerebral vasculature, where blood flow and blood volume were augmented. Or third, there may have been a diminished drug effect in Group I due to a lower acute cerebral drug level.

When SNP was given rapidly to normocarbic/normoxic (Group IIa) animals, the mean ICP increased 18.6 torr above control levels. This ICP response could
be attenuated, but not totally prevented, by two known cerebral vasoconstrictive maneuvers, i.e., hyperventilation and hyperoxegenation. In 1972, Adams et al. confirmed that halothane, as a potent vasodilator, could aggravate intracranial hypertension. They also demonstrated that prior hyperventilation could minimize this influence.

In summary, we conclude that, when SNP is chosen to control systemic pressure in the presence of intracranial hypertension or decreased intracranial compliance, the best and worst circumstances for its infusion can be described: at worst, the drug is rapidly infused under normocarbic/normoxic conditions, while, at best, it is administered slowly to a hypocarbic/hyperoxic individual.

References


Fig. 3. Mean (±SE) effects of rapid sodium nitroprusside administration (over 2 min) on ICP, BP, and CPP in a, normocarbic/normoxic, b, hypocarbic/hyperoxic, and c, hypocarbic/normoxic animals. Absolute BP decreases and CPP were comparable in all subgroups. The greatest ICP increase from control was recorded for Group IIa animals.