

# The Technique of Nitroprusside Administration Modifies the Intracranial Pressure Response

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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 ( $14.8 \pm 1.2$  torr) secondary to inflated epidural balloons. The rate of SNP infusion and the  $Pa_{iO_2}$  and  $Pa_{iCO_2}$  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  $CO_2$  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 IIa animals had the largest average ICP increase ( $18.6 \pm 3.7$  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 hypocarbia and hyperoxia. (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.<sup>1-3</sup> 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.

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A tracheostomy was performed and the lungs were ventilated with a Harvard volume respirator. Respiratory control was facilitated by incremental intravenous doses of gallamine triethiodide, 10–20 mg. A femoral artery and vein were cannulated for continuous blood pressure and intermittent arterial blood-gas monitoring and for drug infusions. End-tidal  $CO_2$  was continuously recorded by a Beckman LB-2 capnograph.

The animals were then positioned in a stereotaxic headholder. Four brass screws were implanted in the four quadrants of the calvarium and served as electrodes for continuous electroencephalographic (EEG) recording. During SNP infusions, polygraph speeds were increased to detect EEG changes. Through bilateral burr holes, posterior to the coronal sutures, two small balloons were introduced into the epidural space, one for expansion and the other for ICP recording purposes. In a few animals, a specially designed hollow epidural screw was substituted for the ICP recording balloon.<sup>4</sup> A watertight seal of the cranial vault was obtained with a methylmethacrylate polymer in a manner previously described.<sup>5</sup> Arterial and intracranial pressures were recorded with Statham P231D® transducers, zeroed at heart level. Mean values were derived by electrical integration and, along with all other variables, were displayed on a polygraph.

The ICP was then increased to  $14.8 \pm 1.2$  torr ( $\pm$ SEM) by incremental inflation of the appropriate epidural balloon with saline solution. Intracranial compliance was considered compromised when a 90-sec inhalational challenge with carbon dioxide, 5 per cent, in oxygen, produced a minimum of a 4 torr increase in ICP. This test also indicated that cerebrovascular reactivity to  $CO_2$  was retained.<sup>6</sup> After each intracranial compliance determination, the arterial blood-gas values were returned to baseline.

The animals were next divided into two major groups, based upon the infusion rate of SNP (0.1 per cent solution) delivered by a Harvard® pump. The first group (I) received a slow, constant infusion sufficient to sustain a 60–70 torr decrease in mean arterial blood pressure over a 5-min period. The second group (II), received a rapid administration of the drug, achieving similar levels of hypotension over a 2-min period. Adjustments in arterial oxygen and carbon dioxide tensions further subdivided the major groups (table 1). Groups Ia and IIa, each consisting of eight

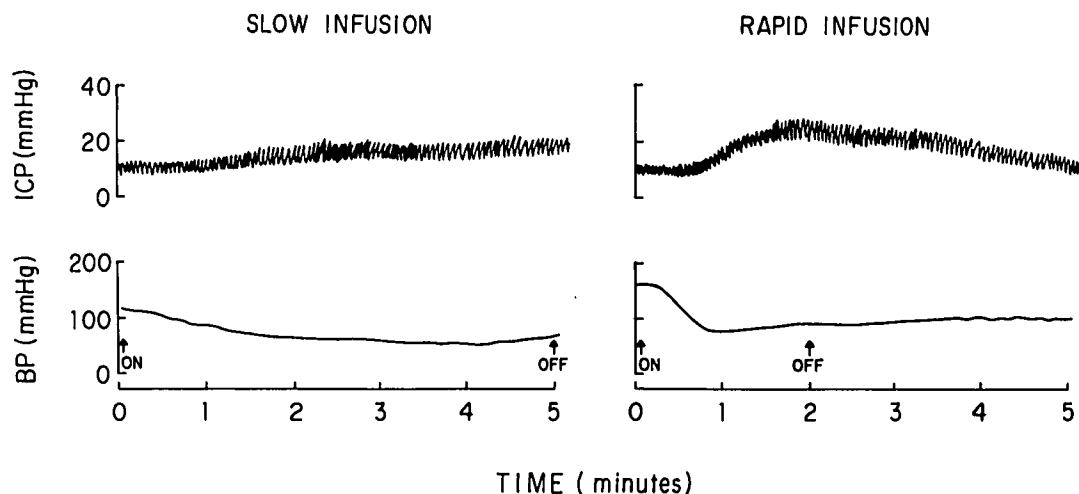


FIG. 1. Comparison of intracranial pressure (ICP) and blood pressure (BP) effects of sodium nitroprusside administered slowly (*a*, left) and rapidly (*b*, right) in two cats. ↑ arrow indicates beginning and termination of infusion. Similar levels of hypotension are achieved by either infusion technique;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

cats, breathed room air ( $P_{aO_2}$   $103 \pm 5$  torr) at normocarbica ( $P_{aCO_2}$   $33 \pm 2$  torr). Groups *Ib* and *IIf*, represented by five and seven cats, respectively, inspired 100 per cent oxygen, and their lungs were hyperventilated ( $P_{aO_2}$   $427 \pm 13$  torr,  $P_{aCO_2}$   $22 \pm 2$  torr). Last, Group *IIf* breathed room air during hyperventilation ( $P_{aO_2}$   $103 \pm 5$  torr,  $P_{aCO_2}$   $22 \pm 2$  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,  $440 \pm 25$   $\mu\text{g/kg/min}$  in Group *I* and  $470 \pm 30$   $\mu\text{g/kg/min}$  in Group *II*, though markedly greater than clinical requirements, were anticipated from previous laboratory trials.<sup>¶</sup> 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 ( $\Delta\text{ICP} = 8$  torr) (fig. 1). As ICP increased, the intracranial systolic-diastolic pulse pressure also increased. In Group *II*, as blood pressure was decreased ICP increased precipi-

tously (fig. 1*b*;  $\Delta\text{ICP} = 15$  torr). Unlike the Group *I* animals, these cats experienced appreciable end-tidal  $\text{CO}_2$  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 ( $\text{CPP} = \text{BP} - \text{ICP}$ ) 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

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

	Infusion Rate	$P_{aCO_2}$ (torr)	$P_{aO_2}$ (torr)
Group <i>Ia</i>	Slow	$33 \pm 2$	$103 \pm 5$
Group <i>Ib</i>	Slow	$22 \pm 2$	$427 \pm 13$
Group <i>IIa</i>	Rapid	$33 \pm 2$	$103 \pm 5$
Group <i>IIb</i>	Rapid	$22 \pm 2$	$427 \pm 13$
Group <i>IIc</i>	Rapid	$22 \pm 2$	$103 \pm 5$

\* Slow infusion occurred over a 5-min period ( $\bar{X}_{\text{dose}} = 440 \pm 25$   $\mu\text{g/kg/min}$ ); rapid infusion lasted 2 min ( $\bar{X}_{\text{dose}} = 470 \pm 30$   $\mu\text{g/kg/min}$ ). Both rates achieved BP decreases of 60–70 torr from the control level. Means ( $\pm\text{SEM}$ ) are indicated.

¶ Keykhah MM, Shapiro HM, Van Horn K, et al: Intracranial pressure response to nitroprusside during progressive intracranial hypertension (abstr), Annual Meeting of the American Society of Anesthesiologists, October 1976, pp 243–244.

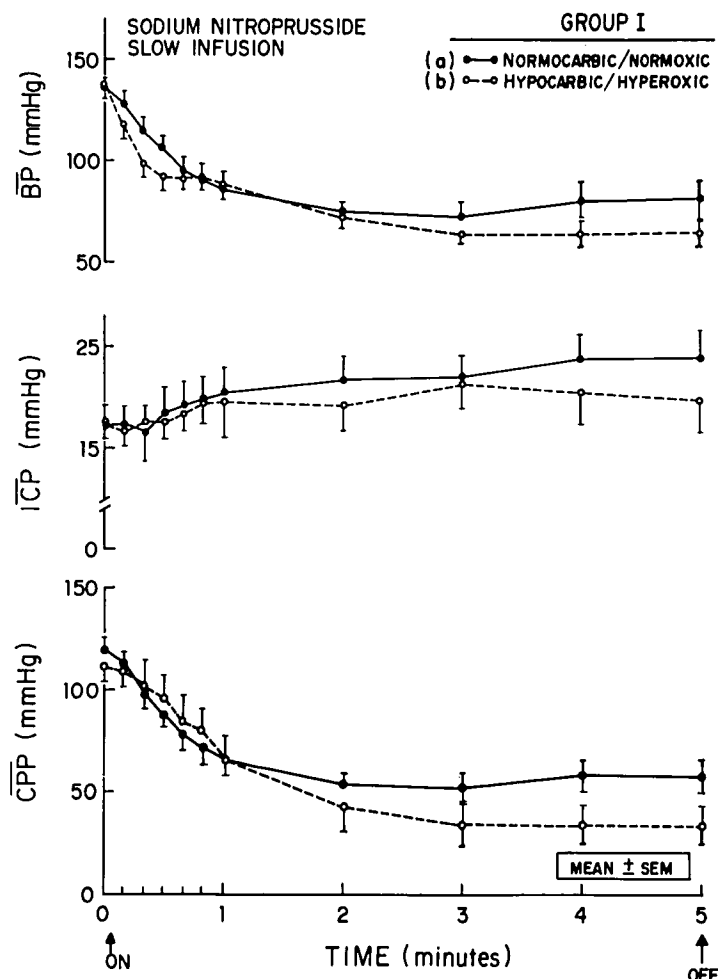


FIG. 2. Mean ( $\pm$ SE) effects of slow sodium nitroprusside infusion (over 5 min) on mean intracranial pressure (ICP), blood pressure (BP), and cerebral perfusion pressure (where  $CPP = BP - ICP$ ) in *a*, normocarbic/normoxic versus *b*, hypocarbic/hyperoxic animals. There was no significant difference between these subgroups.

subgroups, Group IIa had a higher initial blood pressure. This group sustained the earliest and greatest ICP increases ( $18.6 \pm 3.7$  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 ( $\Delta ICP > +8$  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  $CO_2$  reactivity by the inhalation of carbon dioxide. This maneuver also demonstrated a decrease of intra-

cranial 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 tensions.<sup>7</sup>

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 hyperoxygenation. In 1972, Adams *et al.* confirmed that halothane, as a potent vasodilator, could aggravate intracranial hypertension.<sup>8</sup> 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

1. Turner JM, Powell D, Gibson RM, et al: Intracranial pressure changes in neurosurgical patients during hypotension induced with sodium nitroprusside or trimethaphan. *Br J Anaesth* 49:419-425, 1977
2. Cottrell JE, Patel K, Turndorf H: Intracranial pressure changes induced by sodium nitroprusside in patients with intracranial mass lesions. *J Neurosurg* 48:329-332, 1978
3. Marsh ML, Shapiro HM, Smith RW, et al: Changes in neurologic status and intracranial pressure associated with sodium nitroprusside administration. *ANESTHESIOLOGY* 51:336-338, 1979
4. Vries JK, Becker DP, Young HF: A subarachnoid screw for monitoring intracranial pressure. *J Neurosurg* 39:416-419, 1973
5. Aidinis SJ, Lafferty J, Shapiro HM: Intracranial pressure responses to PEEP. *ANESTHESIOLOGY* 45:275-286, 1976
6. Vapalahti M: Intracranial pressure, acid-base status of blood and cerebrospinal fluid and pulmonary function in the prognosis of severe brain injury (Thesis), University of Helsinki, Helsinki, Finland, 1970
7. Cullen DJ, Eger EI II: Cardiovascular effects of carbon dioxide in man. *ANESTHESIOLOGY* 41:345-349, 1974
8. Adams RW, Gronert GA, Sundt TM, et al: Halothane, hypocapnia, and cerebrospinal fluid pressure in neurosurgery. *ANESTHESIOLOGY* 37:510-517, 1972

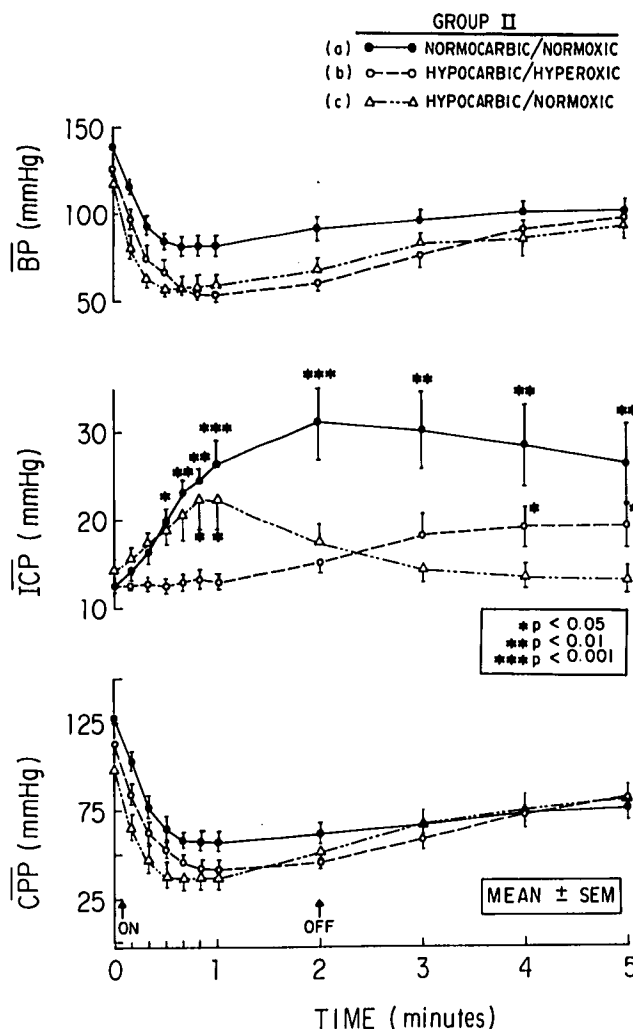


FIG. 3. Mean ( $\pm$ SE) effects of rapid sodium nitroprusside administration (over 2 min) on  $\overline{ICP}$ ,  $\overline{BP}$ , and  $\overline{CPP}$  in *a*, normocarbic/normoxic, *b*, hypocarbic/hyperoxic, and *c*, hypocarbic/normoxic animals. Absolute BP decreases and CPP were comparable in all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