

Title : Nitroglycerin and Nitroprusside Induced Changes in Cerebral Hemodynamics

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Introduction. Nitroglycerin has recently been used as an intravenous vasodilator for controlled hypotension during anesthesia,¹ for congestive heart failure,² and for relief of cerebral vasospasm following subarachnoid hemorrhage.³ However, nitroglycerin has also been shown to raise intracranial pressure⁴ and this raises serious questions about cerebral blood flow changes associated with nitroglycerin. We evaluated the cerebral hemodynamic changes associated with administration of both nitroglycerin and nitroprusside.

Methods. In 5 pentobarbital anesthetized and mechanically ventilated dogs, cerebral blood flow (CBF) was measured by the venous torcular technique.⁵ Blood flow from the confluence of the sagittal straight and lateral sinuses was measured after extracerebral communications were prevented by occlusion of the lateral sinuses. Cerebral spinal fluid pressure (Pcsf) was measured via a catheter placed in the lateral ventricle or cisterna magna. Arterial blood pressure, common carotid blood flow, and arterial and cerebral venous blood gases were measured. Nitroglycerin and nitroprusside were administered in doses of 5, 25, and 50 ug/kg given IV over 30 seconds in random order. Ten to 15 minutes were allowed between each dose of drug so that all parameters could return to control before subsequent administration of drugs. Following the administration of these drugs, Pcsf was artificially elevated by the administration of mock CSF into the lateral ventricle to elevate Pcsf to 30-40 mm Hg and the drugs given again.

Results. The effects of the administration of nitroglycerin and nitroprusside on Pcsf and CBF at normal and artificially elevated Pcsf are shown below. Pcsf values are in mmHg and CBF value are in ml/min. Data is expressed as mean \pm SE. They are expressed as pre-drug and post drug administration values. * = $p < 0.05$

NORMAL PCSF					
5 ug/kg		25 ug/kg		50 ug/kg	
PRE	POST	PRE	POST	PRE	POST
Nitroglycerin					
Pcsf-	11 \pm 3	20 \pm 4 *	12 \pm 3	30 \pm 6 *	11 \pm 3
CBF -	25 \pm 2	26 \pm 3	24 \pm 1	23 \pm 2	24 \pm 2
Nitroprusside					
Pcsf-	12 \pm 2	17 \pm 4 *	18 \pm 3	27 \pm 6 *	13 \pm 5
CBF -	22 \pm 1	22 \pm 1	23 \pm 1	21 \pm 1	24 \pm 3
ELEVATED PCSF					
Nitroglycerin					
Pcsf-	36 \pm 7	54 \pm 12 *	37 \pm 5	58 \pm 7 *	34 \pm 6
CBF -	23 \pm 1	21 \pm 1	21 \pm 1	18 \pm 2 *	22 \pm 1
Nitroprusside					
Pcsf-	39 \pm 1	49 \pm 2 *	35 \pm 7	48 \pm 10 *	28 \pm 13
CBF -	20 \pm 1	20 \pm 1	22 \pm 1	16 \pm 3 *	24 \pm 1

Cerebral perfusion pressure (CPP) fell in all animals after each administration of either nitroglycerin or nitroprusside. In the elevated Pcsf group, however, 25 ug/kg of nitroglycerin lowered CPP to 63 \pm 16 mm Hg while 50 ug/kg nitroglycerin lowered CPP to 56 \pm 11 mm Hg. Also in the elevated Pcsf group, 25 ug/kg of nitroprusside lowered CPP to 57 \pm 13 mm Hg and 50 ug/kg lowered CPP 32 \pm 14 mm Hg. All these changes are statistically significant ($p < 0.05$). It was in these animals with very lowered CPP that the decreases in CBF occurred.

Discussion. These studies document that both nitroglycerin and nitroprusside are capable of elevating Pcsf, lowering cerebral perfusion pressure, and decreasing CBF. The increase in Pcsf appears to be independent of changes in CBF since marked increases in Pcsf occurred with no changes in CBF in the normal Pcsf group. This suggests the possibility that these drugs may increase cerebral blood volume and Pcsf via changes in cerebral venous capacitance. From a clinical perspective these studies confirm that both nitroglycerin and nitroprusside, in the presence of an initially elevated Pcsf, may lower cerebral blood flow. Since the patients most likely to receive these drugs often have marginal cerebral perfusion pressure to start, special attention must be paid to the cerebral hemodynamic effects of these agents. Finally, while producing less systemic hypotension, at any given dose range administered nitroglycerin appeared to elevate Pcsf more than did nitroprusside.

References

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