

Title: VASOPRESSORS DO NOT INCREASE CEREBRAL CORTICAL BLOOD FLOW IN ENDOTOXIN SHOCK

Authors: C.F. Miller, M.D., M.J. Breslow, M.D., S.D. Parker, M.D., A.T. Walman, M.D. and R.J. Traystman, Ph.D.

Affiliation: The Department of Anesthesiology/Critical Care Medicine, The Johns Hopkins Medical Institutions, Baltimore, MD 21205

Introduction. Cerebral blood flow (CBF) is markedly reduced during experimental endotoxin shock (ES).¹ Although raising mean arterial blood pressure (MAP) in ES is a frequent clinical goal, the CBF response to MAP elevation in ES is unknown. We measured total and regional CBF during ES before and after raising MAP with vasopressors.

Methods. Seventeen pigs (45-55 kg) were sedated with ketamine (9-10 mg/kg, IM), anesthetized with pentobarbital (20-30 mg/kg, IV), and maintained nonparalyzed on a continuous infusion of pentobarbital. In the supine position, ventilation was controlled via tracheostomy to maintain a constant P_aCO_2 (38-42 mm Hg). Left ventricular (LV), abdominal aortic, thermodilution pulmonary artery, and central venous catheters were placed. CBF was measured by the radiolabelled microsphere technique (15 micron diameter microspheres) using the LV catheter for injection and the abdominal aortic catheter for withdrawal of reference samples. Thermodilution cardiac outputs (CO) were measured in triplicate by manual injection of iced (0°C) saline (5 cc). Arterial and central venous pressures (CVP) were recorded on a continuous 8-channel strip recorder (Gould) and measurements were taken at end expiration. Endotoxin shock (MAP = 50 mm Hg) was induced in all animals with *E. coli* endotoxin (0.2 mg/kg) infused over 40 minutes. Fluids were given to maintain a constant CVP. CBF, arterial blood gases (ABG), and hemodynamic measurements were obtained before endotoxin (control) and after 60 minutes of ES. Animals were then randomized to receive an intravenous infusion of either norepinephrine (n = 6), dopamine (n = 5) or phenylephrine (n = 6) in doses sufficient to raise MAP to 70-80 mm Hg. CBF, ABG, and hemodynamic data were obtained after 30 minutes of treated shock (Rx). Animals were sacrificed and the brain was sectioned into neuroanatomic regions including cerebral cortex, cerebellum and brainstem. Total and regional flows were determined and the data analyzed by analysis of variance. A p value less than or equal to 0.05 was considered significant. Data are expressed as mean \pm SEM.

Results. Norepinephrine, dopamine and phenylephrine affected CBF similarly in all brain regions and data for these vasopressor groups are pooled into a single group (Rx). Arterial blood gases (ABG) and hemodynamic data are shown in Table 1. P_aO_2 , pH, MAP, and systemic vascular resistance (SVR) decrease with shock. MAP, CO, and SVR are increased with Rx. CBF (ml/min/100 gm) for whole brain and for regional brain areas are shown on Table 2. CBF decreased with shock in all regions. CBF to cerebellum and brainstem, in contrast to other regions, increased with Rx.

Discussion. The decreases in regional CBF with ES are similar to those reported by others.¹ Unchanged cortical CBF after Rx suggests either (1) an inability to autoregulate or (2) disruption of the blood brain barrier resulting in vasopressor induced vasoconstriction which limits flow. Regardless of mechanism, failure to restore cortical flow may contribute to cerebral ischemia during ES. In contrast to cerebral cortical flow, CBF to cerebellum and brainstem is restored to control values with Rx. This response may reflect underlying structural heterogeneity of the cerebral vasculature which permits restoration of flow to the cardio-respiratory regulatory centers.

Reference.

1. Bryan WJ, Emerson TE: Blood flow in seven regions of the brain during endotoxin shock in the dog (39907). Proc Soc Exp Biol and Med 156: 205-208, 1977

TABLE 1 (n = 17): Hemodynamic and Blood Gas Data

	Control	Shock	Rx
P_aCO_2	39.7 \pm 0.8	41.4 \pm 0.7	41.6 \pm 1.0
P_aO_2	412 \pm 11	224 \pm 30*	116 \pm 25*
pH	7.44 \pm 0.01	7.34 \pm 0.01*	7.32 \pm 0.01*
Hgb	9.9 \pm 0.4	10.9 \pm 0.5	10.6 \pm 0.3
MAP	126 \pm 3	50 \pm 2*	74 \pm 1**
CO	4.8 \pm 0.5	3.7 \pm 0.4	4.7 \pm 0.3**
CVP	4.1 \pm 0.6	4.1 \pm 0.5	4.7 \pm 1.1
SVR	25.6 \pm 4	13.1 \pm 1.0*	15.8 \pm 1.0**

Units of Measurement: P_aCO_2 , P_aO_2 , MAP and CVP torr; Hgb gm/dL; CO L/min.

* p < 0.05 compared to control

** p < 0.05 compared to shock

TABLE 2 (n = 17): Total and Regional CBF

	Control	Shock	Rx
Brain (total)	37.8 \pm 2.9	25.2 \pm 3.1*	27.1 \pm 2.8*
Cortex	36.1 \pm 2.7	22.9 \pm 2.8*	26.3 \pm 2.8*
Cerebellum	47.0 \pm 3.6	30.8 \pm 4*	40.9 \pm 4.9**
Brainstem	35.9 \pm 3.1	24.3 \pm 2.6*	41.8 \pm 4.7**

* p < 0.05 compared to control

** p < 0.05 compared to shock