TITLE: HYPOCAPNIA AND HYPERCAPNIA CAUSE HETEROGENEOUS CHANGES IN REGIONAL ORGAN BLOOD FLOW

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Although the cerebrovascular and myocardial effects of carbon dioxide (CO_2) have been extensively studied, there is little data regarding its effects on other organs. Furthermore, previous studies evaluating regional hemodynamic effects of CO_2 have been complicated by changes in the mechanics of ventilation.[1] Accordingly, the present study was performed to evaluate regional blood flow responses to arterial CO_2 tensions ($PaCO_2$) in the absence of alteration in mechanical ventilation.

Fifteen mongrel dogs were anesthetized with 0.9% halothane in oxygen (1 MAC) while mechanically ventilated to maintain $PaCO_2$ equal to 40 mmHg. Mean arterial pressure (MAP) was measured via a cannula positioned in the thoracic aorta. Regional organ blood flow (RBF; in ml/min/100g) was measured with 15μ radioactive microspheres under control conditions (n=15) and during either hypocapnia (n=8) or hypercapnia (n=7), induced by adding or removing deadspace attached to the endotracheal tube. Statistical analyses were performed with Student's t-test for paired samples.

Changes in RBF are presented in Table 1. Hypocapnia ($PaCO_2$, 22±1 mmHg) decreased blood flow in the myocardium (-17%), brain (-32%), kidney (-19%), duodenum (-32%), spleen (-52%), and skin (-44%) but had no significant effect on flow in the pancreas or skeletal muscle. Hypercapnia ($PaCO_2$, 67±4 mmHg) increased blood flow in the brain (+158%) and duodenum (+100%), decreased blood flow in skeletal muscle (-67%), and had no significant effect on flow in other organs. Neither hypo- or hypercapnia had significant effects on MAP.

Conclusions: 1) Both hypo- and hypercapnia caused heterogeneous changes in RBF. 2) Regional vasomotor effects of hypercapnia were opposite to hypocapnia in only selected organs. These findings may be explained by regional differences in the responsiveness of vascular smooth muscle to direct effects of CO_2 and/or regional differences in the influence of neurohumoral mechanisms.

References

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Table 1. Effects of $PaCO_2$ on RBF (ml/min/100g)

	Control	Hypocapnia	Hypercapnia
Myocardium	54 ± 4	45 ± 4*	50 ± 3
Brain	50 ± 3	34 ± 2*	129 ± 14*
Kidney	540 ± 28	439 ± 56*	462 ± 50
Duodenum	40 ± 3	27 ± 2*	80 ± 16*
Spleen	163 ± 13	78 ± 9*	181 ± 30
Pancreas	15 ± 2	14 ± 2	11 ± 1
Sk. Muscle	3.0 ± 0.5	3.3 ± 0.4	1.3 ± 0.3*
Skin	2.5 ± 0.3	1.4 ± 0.2*	2.4 ± 0.5

Values are Mean ± S.E. * $P < 0.05$ from Control

ACUTE VASODILATORY EFFECT OF TUMOR NECROSIS FACTOR (TNF) ON THE RABBIT CAROTID ARTERY.

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TNF is believed to be one of the major mediators of sepsis. Decrease in vascular resistances and hyporesponsiveness to contractile agonists are commonly observed in septic shock. We have therefore examined the vascular effects of recombinant human TNF (rTNF) on the precontracted rabbit carotid artery. The two carotids, excised at in vivo length and physiological pressure, were incubated in oxygenated Krebs-Ringer solution at a transmural pressure of 90 mmHg. Changes in diameter were measured using an ultrasonic microdimensiometer. Contractions were induced by extraluminal phenylephrine (PE) at $7x10^{-7}$ M, or KCl at 60 mM. rTNF was then added in the extraluminal solution to give a concentration from 0.01 to 0.7 µg/ml. As shown in the figure, rTNF elicited a dose-dependent relaxation of PE-contracted carotids, with an IC_{50} of 3.2 nM. This relaxation was immediate, and the mean maximal vasodilation was 79.3 ± 5.9 % of the initial contraction. This effect was almost completely abolished by methylene blue (MB, 10^{-5} M), an inhibitor of the soluble guanylate cyclase. No vasodilatory effect was observed after KCl-induced contractions. Four carotids were also tested after exposure to N-monomethyl-L-arginine (NMMA) at $3x10^{-4}$ M, an inhibitor of L-arginine pathway, to test whether this effect was mediated by nitric oxide production from L-arginine. Preexposure to NMMA did not alter the relaxing effect of rTNF.

This study shows an acute vasodilatory effect of rTNF on the PE-precontracted rabbit carotid, which seems to be due to a direct activation of the guanylate cyclase of vascular smooth muscle. Inhibition of smooth muscle cell contraction by prolonged exposure to Interleukin-1 and TNF has also been reported[1,2]. These results suggest that cytokines might mediate the vascular tone defect observed in septic shock.

References

1. J Clin Invest 83:331-335, 1989.
2. FASEB J. 4:A1111, 1990.