Title: CEREBROVASCULAR RESPONSE TO HYPOTENSION: EFFECT OF ANTIHYPERTENSIVE THERAPY

Authors: W.E. Hoffman, Ph.D., D.J. Miletich, Ph.D., and R.F. Albrecht, M.D.

Affiliation: Department of Anesthesiology, Michael Reese Hospital and Medical Center, Chicago, Illinois

Introduction. It is known that hypertension produces a shift in the cerebral autoregulatory curve with the lower limit of autoregulation shifted to a higher blood pressure (1). In these experiments we have tested the ability of antihypertensive therapy to reverse these changes in the spontaneously hypertensive rat (SHR) and decrease the risk of cerebral ischemia during hypotensive anesthesia.

Methods. Thirty male 4 month old SHR and 30 male 4 month old Wistar Kyoto (WKY) normotensive controls were used in these experiments. Fifteen rats in each group received 10 weeks of antihypertensive therapy and 15 received 10 weeks of sham treatment. Antihypertensive therapy consisted of 2 mg/kg/day minoxidil, 8 mg/kg/day hydralazine and 8 mg/kg/day propranolol given in the drinking water. Tail systolic blood pressure was measured 1-2 times per week in each antihypertensive and sham treated rat over the 10 week treatment period. After 10 weeks of antihypertensive or sham treatment, cerebral blood flow (CBF) and cerebral oxygen consumption ($CMRO_2$) were measured randomly in each rat under control anesthetized conditions (1.25 mg/kg/min ketamine iv) or during sodium nitroprusside (SNP) induced hypotension to levels of 80-85 torr (mid level) or 50-55 torr (low level). CBF was measured in each test using radioactive microspheres and $CMRO_2$ was calculated as CBF multiplied by arterial-sagittal sinus oxygen content. Arterial PCO_2 was maintained at 35-40 torr with artificial ventilation and body temperature at 37C in all experiments.

Results. Sham treatment produced no significant change in tail systolic blood pressure in SHR or WKY over the 10 week treatment period. Antihypertensive therapy decreased blood pressure approximately 30% in both SHR and WKY over the 10 weeks. Blood pressure decreased in drug treated SHR to similar levels seen in sham treated WKY. Cerebrovascular response to SNP induced hypotension is shown in Table 1. CBF decreased significantly in sham treated SHR at both levels of SNP induced hypotension. In sham and drug treated WKY and antihypertensive treated SHR CBF was maintained at the mid but not the low SNP induced pressure level. Cerebral autoregulation was significantly improved in SHR following antihypertensive therapy but was still different from normotensive WKY.

Discussion. Data presented here agree with a previous report indicating that SNP induced hypotension will not maintain CBF or $CMRO_2$ in hypertensive rats (2). Autoregulation of CBF was significantly improved in SHR receiving antihypertensive therapy but differences were still apparent compared with normotensive WKY. These results indicate altered cerebrovascular performance in SHR during SNP induced hypotension and the importance of antihypertensive therapy in reversing these changes.

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References.

1. Kety S, King B, Feffers S, et al: The effects of acute reduction in blood pressure by means of sympathetic block on the cerebral circulation of hypertensive patients. J. Clin. Invest. 29:402-416, 1950.

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TABLE 1
CEREBROVASCULAR CHANGES IN SHR AND WKY
DURING SNP INDUCED HYPOTENSION

		BP	CBF	$CMRO_2$	n
Sham treated WKY	con	120±4	134± 6	6.9±.3	1
	mid	88±2*	125± 8	6.9±.5	1
	low	54±2*	89± 8*	5.8±.5	1
Antihypertensive treated WKY	con	94±6	139±14	6.4±.5	1
	mid	82±2*	146± 8	6.9±.5	
	low	55±2*	91± 4*	5.5±.4	1
Sham treated SHR	con	180±6	119± 6	6.2±.4	
	mid	92±2*	61± 9*	5.7±.6	1
	low	58±2*	37± 5	3.5±.5*	
Antihypertensive treated SHR	con	139±3	107±12	5.1±.7	
	mid	91±2*	102±13	5.3±.8	
	low	56±2*	55± 5*	3.5±.3*	1

* = $p<.05$ compared to control values

units: BP=mmHg, CBF=ml/100g/min, $CMRO_2$=ml O_2/100g/min