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INTRODUCTION: The role of the microcirculation in the etiology of hypertension is largely unknown. From experimentation with the spontaneously hypertensive rat (SHR) numerous hypotheses have been formulated to explain the involvement of the microcirculation in hypertension including decreased arterial diameters (1,2), arterial rarification (3), and hyperresponsiveness to catecholamine vasoconstrictors (4). The response of each of these parameters to vasoactive substances has been studied as single components, i.e. changes in arterial diameter or microvessel blood pressure (micropressure), but not in terms of vascular resistance, which is one of the main determinants of the elevated blood pressure as seen in the SHR. Unless the vascular resistance is known, conclusions cannot be made about the contribution of the microcirculation to the hypertensive state. Thus, the objectives of this study were to: (1) compare the vascular resistance of the SHR and its normotensive counterpart, (2) determine if elevated vascular resistance responses were evident during exposure to alpha-adrenergic stimulation, and (3) determine if the presence of topically induced vasodilation could significantly alter the purported elevated responses to alpha-adrenergic stimulation.

METHODS: Changes in the microvascular input resistance (MVR) of the microvasculature distal to the first order arteries following graded concentrations of topically applied norephinephrine (NE) (a catecholamine) and phenylephrine (PE) (a non-catecholamine) were used to determine the presence and extent of augmented alpha-adrenergic pharmacological sensitivity in the spontaneously hypertensive rat (N=8) as compared to the normotensive (WKY) rat (N=8). NE was also subsequently superfused over the preparation in the presence of nitroprusside (NP) (10^{-5}M), a non-alpha-receptor mediated vasodilator. MVR was calculated as the ratio of second order (2A) microvessel blood pressure (servo-null method) to 2A blood flow (dual-slit method) for the cremaster muscle microcirculation.

RESULTS: The following table illustrates the changes in microvascular resistance in response to superfused graded concentrations of the alpha-adrenergic agonists NE and PE. NE was also superfused in the presence of a fixed 10^{-5}M concentration of NP.

Microvascular Resistance (mmHg/nl/sec)

NE x 10^{-8}M	0.0	0.2	0.5	1.0	2.0	5.0	10.0	20.0
WKY	0.4	0.4	0.4	0.5	0.7	2.2	-	-
SHR	1.5	2.2	3.4	5.0	7.6	9.3	-	-
WKY-NP	0.3	-	-	-	0.3	0.4	0.6	0.9
SHR-NP	0.5	-	-	-	0.9	1.4	1.9	3.8

PE x 10^{-6}M	0.0	0.5	1.0	2.0	0.5	10.0	20.0	50.0
WKY	0.2	0.4	0.6	0.9	2.8	5.5	11.9	-
SHR	0.9	2.0	3.0	7.0	27.3	-	-	-

All SHR-WKY differences are significant ($P<0.05$)

DISCUSSION: The data indicate that the elevated total peripheral resistance as seen in SHR whole body measurements is due in part to an elevated MVR present in the microvasculature in the control state and following both NE and PE challenge. The maximally dilating concentration of NP reduced the difference in MVR between the two groups but did not totally eliminate it. This lack of equalization of MVR values upon maximal vasodilation would indicate that properties other than simple vasoconstriction or a decrease in the number of arterioles open to flow are responsible for the elevated resistance. Other possibilities include structural differences in the arteries (2) and vessel rarification (3). The NE challenge in the presence of NP showed similar trends in the MVR relationship between SHR and WKY (compared to the undilated state). This would indicate that in spite of the elimination of all inherent vasoconstriction normally present, the greater MVR responses were elicited from the SHR. Thus, it is concluded that the SHR demonstrated elevated MVR responses, compared to the WKY, to both catecholamine (NE) and non-catecholamine (PE) alpha-adrenergic stimulation and plays in integral part in the elevated microvascular resistance seen in the SHR.

REFERENCES:
1. Harper RN, Moore MA, Marr MC, Watt LE, Hutchins PM: Arteriolar rarefaction in the conjunctiva of human essential hypertensives. Microvasc Res 16:369-372, 1978.
2. Roy JW, Mayrovitz HN: Microvascular blood flow in the normotensive and spontaneously hypertensive rat. Hypertension 4:264-271, 1982.
3. Hutchins PM, Darnell AE: Observation of a decreased number of small arterioles in spontaneously hypertensive rates. Circ Res 34 α 35(I):161-165, 1974.
4. Bohlen HG: Artrial closure mediated by hyperresponsiveness to norepinephrine in hypertensive rats. J Appl Physiol: 236(1):H157- H164, 1979.

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