



Role of circulating adrenaline in the pathogenesis of hypertension

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SUMMARY

As adrenaline (AD) contributes to the high blood pressure levels associated with acute stress much attention has focused on a possible role of chronic elevations of circulating AD in the pathogenesis of hypertension. In this thesis, the relationship between circulating AD and blood pressure has been examined.

Aortic catheters were implanted in spontaneously hypertensive rats (SHR) and stroke-prone SHR (SHRSP) and genetically related (Wistar Kyoto (WKY)) and unrelated (Black-hooded Wistar (BHW) and Sprague Dawley (SD)) normotensive rats, to determine mean arterial pressure (MAP) and plasma catecholamine levels in a conscious and unrestrained state.

At 5-7 weeks of age, MAP was already elevated in the hypertensive strains compared with WKY or SD rats. Plasma AD was higher (76%) in SHR and lower in SD compared to WKY. In adult rats (7-9 months of age), MAP was higher in the hypertensive strains than in WKY. Circulating AD levels were 3-4 times higher in the hypertensive rats but did not differ between normotensive strains.

Plasma catecholamine levels were also measured in WKY hyperactive (WK-HA) and WKY hypertensive (WK-HT) strains to determine if plasma AD is related to the hyperactivity trait of SHR. Catecholamine levels did not differ between strains, indicating that the elevation of plasma AD in the hypertensive rats is not attributable to their hyperactivity.

The relationship between blood pressure and plasma AD was examined by modifying AD levels in normotensive and hypertensive rat strains. Chronic minipump AD infusion did not effect MAP in WKY, even though plasma AD levels were elevated 12 fold. Ten weeks after adrenalectomy in SHRSP, plasma AD was reduced by 34% and MAP was slightly higher in these rats.

These results imply that circulating AD is not a determinant of resting blood pressure. The possibility that elevated AD levels may be a consequence of hypertension was addressed by chronically altering blood pressure levels in WKY and SHRSP. WKY were

made hypertensive by administration of a nitric oxide synthesis inhibitor (L-NAME). Blood pressure was lowered in SHRSP by chronic administration of hydralazine.

Chronic L-NAME treatment in WKY, significantly elevated MAP. This hypertension was accompanied by a significant increase in circulating AD levels. Conversely, chronic hydralazine treatment in SHRSP, significantly lowered MAP and plasma AD concentrations.

These results suggest that the elevation of circulating AD in hypertensive rats is a consequence rather than a cause of their hypertension.