LETTERS TO THE EDITOR

Adrenergic Reactivity in Low Renin and Normal Renin Essential Hypertension

The article by Lowder, Hamet, and Liddle, "Contrasting Effects of Hypoglycemia on Plasma Renin Activity and Cyclic AMP in Low Renin and Normal Renin Essential Hypertension" (Circ. Res. 38: 105–108, 1976) is testing one of the hypotheses of the mechanism of low renin essential hypertension, the sympathetic dysfunction of the β-adrenergic regulatory system. The authors conclude that the blunted increase in plasma cyclic AMP (cAMP) during hypoglycemia may point to a generalized alteration in β-adrenergic responsiveness in this condition with renin hyporesponsiveness being a part of it. As to the mechanism of this blunted adrenergic responsiveness, it does not differentiate whether the defect concerns the adrenergic receptor sites prior to or after cyclic AMP generation. Most of the catecholamine measurements in low renin hypertension concern only norepinephrine (NE) and are inconclusive. Epinephrine data are therefore of interest, in inconclusive.

We have determined urinary catecholamine excretion in seven patients with low renin essential hypertension characterized similarly as Lowder et al. did, and compared them with 11 patients with normal plasma renin activity (PRA) and 10 control subjects. The suppression of renin was tested by exposing the patients to upright posture and dietary sodium restriction. Low renin essential hypertensive patients, compared to control subjects and normal renin essential hypertensive patients, were found to have significantly elevated urinary epinephrine excretion but no significant differences in NE excretion (Table 1).

This previously unexplained finding may be in two ways related to the finding by Lowder and co-workers: (1) Epinephrine is the endogenous catecholamine with the most evident β-adrenergic receptor action; if the β-adrenergic receptors are hyporeactive, as would be suggested by cAMP responses to insulin hypoglycemia, epinephrine release can be increased by a positive feedback known to exist between the sensitivity of the receptors and catecholamine release. (2) Alternatively, the hypersecretion of epinephrine could be primary and have induced a secondary subsensitivity of the β-adrenergic receptors. A primary hyposensitivity of the receptor sites seems to be more plausible since low renin essential hypertensive patients were shown to be unable to raise PRA in response to NE infusion, and the increased sympathetic activity in response to furosemide, as measured by the excretion rate and plasma concentration of NE, was not accompanied by an increase of PRA in low renin essential hypertensive patients.

Thus, low renin essential hypertension can be considered to be a hyopadrenergic state in which several factors (the hypertension itself, its longer duration, older age of the patients, sodium retention, and in some cases volume expansion) combine to suppress the sympathetic activity. The relative ineffectiveness of β-adrenergic blocking agents in this form of hypertension does not necessarily imply low renin to be its only explanation; it would be well compatible with a hypertensive state in which all β-adrenergic mechanisms are suppressed to a point where postural adaptation and the nerve-dependent renin release deteriorate so that no effect of β-adrenergic blocking agents can be expected. Further concomitant hemodynamic, hormonal, and "second" messenger studies on age- and sex-matched hypertensive subjects will be needed to extend this interesting observation of Lowder and co-workers and its pathophysiological and clinical implications.

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