Response to a New Hormone Therapy With Drospernone and NO Production in Postmenopausal Women

We appreciate Tsuda’s interest in our clinical trial with drospirenone (DRSP) and 17-β estradiol, which demonstrated antihypertensive efficacy in postmenopausal women with stages 1 to 2 hypertension. At this point in time, the effects of DRSP on vascular function can be most appropriately discussed in relation to its effects as an aldosterone antagonist. There is substantial evidence that, in addition to its classical endocrine effects, aldosterone is involved in fibrotic target–organ damage in patients with cardiovascular diseases through intermediate mechanisms involving interactions among the mineralocorticoid receptor, sodium intake, and a variety of molecular messengers. Reductions in mortality that have been achieved in patients with severe heart failure and postmyocardial infarction by the addition of aldosterone receptor antagonists may be examples of the impact of these effects. In addition, studies in animal models treated with the NO inhibitor N^G-nitro-L-arginine methyl ester, angiotensin II, and sodium, with and without adrenalectomy, have demonstrated that myocardial fibrosis can be eliminated by adrenalectomy or by administering an aldosterone receptor antagonist and is induced by adding back aldosterone to adrenalectomized animals. Other animal studies have established that DRSP can reduce blood pressure in male hypertensive rats, whereas conventional progestins increase blood pressure in this model. DRSP has also been shown to prevent hypertension and fetal growth retardation in pregnant rats after the administration of N^G-nitro-L-arginine methyl ester. Taken together, these findings suggest indirectly that DRSP as an antagonist of aldosterone may enhance vascular relaxation in part through enhanced NO availability. Nevertheless, direct assessment of the effects of DRSP on endothelial function in a human hypertensive population has yet to be completed.

Disclosures

W.B.W. is a consultant for Berlex Laboratories.

William B. White
Division of Hypertension and Clinical Pharmacology
Pat and Jim Calhoun Cardiology Center
University of Connecticut School of Medicine
Farmington, Conn


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