Attenuated responses to angiotensin II in follitropin receptor knockout mice, a model of menopause-associated hypertension.

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Abstract

Activation of the renin-angiotensin system has been implicated in the development of hypertension in menopausal women. We investigated whether blood pressure is elevated and whether angiotensin II (Ang II)-induced vascular reactivity is increased in follitropin receptor knockout (FORKO) female mice. These mice are estrogen-deficient and have characteristics similar to postmenopausal women. Serum estradiol levels were significantly reduced in FORKO versus wild-type mice (1.4+/-0.2 versus 15+/-3 pg/mL, P<0.01). Blood pressure, measured by telemetry, was significantly increased in FORKO (120+/-2/92+/-2 mm Hg) compared with wild-type counterparts (110+/-1/85+/-2 mm Hg, P<0.05). Vascular dose responses to acetylcholine (endothelium-dependent dilation) and sodium nitroprusside (endothelium-independent dilation) were not different. Ang II-induced vasoconstriction was blunted in FORKO compared with wild-type mice (P<0.05). Media-to-lumen ratio was significantly increased in FORKO (6.2+/-0.5%) versus control mice (5.2+/-0.3%), indicating vascular remodeling. Aortic*O2- levels, NADH-inducible.O2- generation, and plasma levels of thiobarbituric acid reactive substances (TBARS), indexes of oxidative stress, were not significantly different between wild-type and FORKO mice. Vascular AT1 receptor content, assessed by immunoblotting, was reduced by 40% in FORKO compared with wild-type mice (P<0.01). This was associated with decreased circulating Ang II levels in FORKO versus control mice. These data indicate that FORKO mice have increased blood pressure, vascular remodeling, and attenuated vascular responses to Ang II. Our findings suggest that vascular Ang II signaling is downregulated in female FORKO mice and that Ang II may not play an important role in blood pressure elevation in this model of menopause-associated hypertension.