Response to Testosterone and Sympathetic Nerve Activity During Pregnancy

We are strongly encouraged by the enthusiasm expressed by Dr Carter regarding our recent article. Dr Carter commented that we used a well-controlled experimental model and that it is a novel study that provides critical mechanistic insight and a potential therapeutic target for gestational hypertension, and he emphasized that there is a need for clinical translation of this important work. Further, Dr Carter appreciated the clinical significance of our study and extended its possible implications toward pregnancy-associated obstructive sleep apnea. We thank Dr Carter for his positive comments and his suggestions on the need for simultaneous assessment of sympathetic neural and endothelial function.

Our study demonstrated that elevated maternal testosterone levels cause blunting of endothelial NO-mediated vasodilation and concomitant increases in systemic mean arterial pressure. Dr Carter raises the possibility that testosterone during pregnancy may exacerbate muscle sympathetic nerve activity, which may contribute to blunting of NO-mediated vasodilation and increases in mean arterial pressure. It is likely that a significant interaction exists between testosterone and muscle sympathetic nerve activity in endothelial function. Previous studies show that acute increases in sympathetic activity lead to decreased endothelial function. Men tend to have higher sympathetic outflow than women, who are shown to have higher endothelial NO production, suggesting sex steroids contribute to sympathetic activity regulation. As mentioned by Dr Carter, women with polycystic ovarian syndrome or preeclampsia, known to be associated with decreased endothelial function, have severely increased sympathetic outflow. The increased sympathetic nerve activity in polycystic ovarian syndrome patients was shown to be attributable to the excessive testosterone levels.

Although our studies show that direct exposure of endothelial cells to testosterone in culture leads to decreases in the endothelial NO synthase activity state with decreased nitrate/nitrite production, additional detrimental effects on endothelial cells mediated through enhanced muscle sympathetic nerve activity cannot be discounted. Clearly, as suggested by Dr Carter, additional studies are warranted to confirm whether elevated testosterone exaggerates muscle sympathetic nerve activity and whether it may contribute to endothelial dysfunction and increased arterial blood pressure.

Similarly, as suggested by Dr Carter, it is plausible that testosterone may be a contributing factor for the development of obstructive sleep apnea in preeclamptic patients. It was an interesting suggestion by Dr Carter to determine whether nonpharmacological approaches for obstructive sleep apnea (ie, continuous positive airway pressure) help prevent endothelial and cardiovascular dysfunction associated with elevated testosterone. We thank Dr Carter for his critical suggestions and agree that simultaneous assessment of sympathetic neural and endothelial function is needed and is important for clinical translation of this work.

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Disclosures

None.

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Letter to the Editor
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