Testosterone and Sympathetic Nerve Activity During Pregnancy

To the Editor:

I read with great interest the article by Chinnathambi et al1 that examined the influence of testosterone on the endothelial nitric oxide (NO) system. The role of testosterone in gestational cardiovascular function has not been adequately examined, despite the fact that testosterone levels are exaggerated in preeclamptic and polycystic ovary syndrome pregnancies. Chinnathambi et al1 used a well-controlled experimental model in which pregnant rats were injected with vehicle or testosterone propionate, with the goal of increasing plasma testosterone to mimic levels observed during preeclampsia. The authors report that increased testosterone was associated with elevated blood pressure and blunted NO-mediated vasodilation. This novel study provides critical mechanistic insight and a potential therapeutic target during gestational hypertension.

Several studies suggest that pregnancy is associated with increased levels of muscle sympathetic nerve activity, and evidence is accumulating to suggest that preeclampsia might be linked to circumstances, where this sympathoexcitation is accompanied by dysfunction of vasodilatory mechanisms.2 Moreover, Sverrisdottir et al3 reported that polycystic ovary syndrome was associated with elevated resting muscle sympathetic nerve activity, and that the extent of sympathoexcitation was significantly related to testosterone levels. Therefore, it seems plausible that in addition to impairing NO-mediated vasodilation,1 testosterone might also augment the typical surge of muscle sympathetic nerve activity associated with pregnancy. To date, the influence of testosterone on gestational muscle sympathetic nerve activity has not been adequately examined, and it remains unclear whether abnormally high levels of testosterone worsen the sympathetic storm associated with pregnancy.

In addition, obstructive sleep apnea (OSA) is a recognized risk factor for hypertension. Evidence suggests that pregnancy increases the incidence of OSA, and that preeclampsia may exacerbate OSA severity.4 As highlighted by Chinnathambi et al,1 testosterone is elevated 2-fold during preeclampsia. Recent studies suggest that OSA is also a risk factor for hypertension in polycystic ovary syndrome women compared with weight-matched controls, and that elevated testosterone may play a key role.5 The relations among testosterone, OSA, and pregnancy remain unclear, but it seems reasonable to speculate that testosterone may be a contributing factor to the increased incidence of OSA during preeclampsia. Is it possible that the testosterone treatment in the study by Chinnathambi et al1 increased the incidence of OSA, and that this may have contributed to the rise in arterial blood pressure and blunted NO-mediated vasodilation? Future studies might better define the role of testosterone on the presumed endothelial/cardiovascular dysfunction associated with gestational OSA.

In summary, the study by Chinnathambi et al1 demonstrates that increased testosterone elicits a hypertensive response that is associated with blunted NO-mediated vasodilation in pregnant rats. There is a need for clinical translation of this important work, and future studies might include integrative techniques to simultaneously assess sympathetic neural activity and endothelial function.

Disclosures

None.

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