Response to Are Aldosterone Levels Inappropriately Low in Preeclampsia?

Verdonk et al.1 raise an interesting hypothesis that increased angiotensin II sensitivity and angiotensin II type 1 receptor autoantibodies in preeclampsia may not lead to inappropriately lower aldosterone levels, a hypothesis not supported by both experimental and clinical studies. In humans, aldosterone levels are relatively high throughout gestation in the setting of higher plasma volume.2 In contrast, in subjects with preeclampsia, aldosterone levels are relatively low (when compared with normotensive pregnancy), despite lower plasma volume. In addition, circulating levels of renin and angiotensin II are lower in preeclampsia.3

As noted by Verdonk et al.,1 suppressed renin–angiotensin II–aldosterone levels during preeclampsia are accompanied by enhanced angiotensin II sensitivity in the vasculature. Recently, Siddiqui et al.4 reported that angiotensin II type 1 receptor autoantibodies, which have been implicated in enhancing angiotensin II sensitivity during preeclampsia, directly inhibit aldosterone production by inducing soluble fms-like tyrosine kinase 1 and by causing vascular impairment in adrenal glands. These data support our experimental findings that aldosterone levels are correlated inversely with circulating soluble fms-like tyrosine kinase 1 levels in rodents.5 In summary, aldosterone is lower during preeclampsia because of excess circulating soluble fms-like tyrosine kinase 1. Although aldosterone is lower in preeclampsia when compared with normotensive pregnancy, aldosterone/renin ratios are increased because of even more dramatic suppression of renin production. We speculate that lower renin levels in preeclampsia may also be related to vascular damage to juxtaglomerular fenestrated vasculature because of high circulating soluble fms-like tyrosine kinase 1 levels in preeclampsia.

Disclosures

S.A. Karumanchi is a coinventor of multiple patents on preeclampsia markers. He serves as a consultant to Roche, Siemens, and Beckman Coulter and has financial interest in Aggamin LLC. The other authors report no conflicts.
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