Nongenomic Response to Aldosterone

To the Editor:

It is with great interest that we read the article titled, “GPR30 Expression Is Required for the Mineralocorticoid Receptor–Independent Rapid Vascular Effects of Aldosterone,” by Gros et al.,1 showing that aldosterone at low picomolar concentrations can act rapidly via both GPR30 and classic mineralocorticoid receptors over a range of parameters. These included extracellular signal-regulated kinase 1/2 activation and myosin light chain phosphorylation in rat aortic vascular smooth muscle cells in vitro; for extracellular signal-regulated kinase activation, aldosterone had equivalent action via both receptors at low picomolar concentrations, whereas for myosin light chain phosphorylation, 10 nmol/L of aldosterone for 15 minutes was used.

With regard to its nongenomic vasoconstriction, by directly measuring the internal diameter by video microscopy, we reported that aldosterone (10^{-13} to 10^{-6} M), but not hydrocortisone, produced a dose-dependent vasoconstriction in the mesenteric arterioles (60 to 160 μm) isolated from C57BL/6J mice: the maximal diameter change after aldosterone was −8.6±0.3% from the baseline.2 Notable vasoconstriction occurred at 10 seconds after administration, and the response reached the maximum within a few minutes in almost all of the experiments. The vasoconstrictor effect was unaffected by the mineralocorticoid receptor antagonist spironolactone at 10^{-6} M and eplerenone at 10^{-5} M, the angiotensin II type 2 receptor antagonist PD123319 at 10^{-4} M, and the endothelium denudation. However, aldosterone’s vasoconstrictor effect was negligible in angiotensin II type 1a knockout mice and suppressed by pretreatment with the angiotensin II type 1 blockers valsartan at 10^{-4} M and 10^{-6} M and candesartan at 10^{-7} M. Interestingly, the transglutaminase inhibitors cystamine and monodansyl cadaverine suppressed not only aldosterone’s vasoconstrictor effect but aldosterone-induced formation of angiotensin II type 1 dimer.

We here mention 2 points, which are remarkable in this study. First, myosin light chain phosphorylation related to a nongenomic vasoconstrictor effect of aldosterone was relatively slow and was caused by higher concentration of aldosterone compared with our previous findings obtained from direct measurement of the internal diameter in mesenteric arterioles. Second, these effects were partially but definitely mediated with mineralocorticoid receptor despite the fact that, in our direct measurement, neither spironolactone nor eplerenone affected vasoconstrictor effect of aldosterone. It seems important to clarify whether the disparity of the response to aldosterone is merely attributed to the difference of animal strain and vessels. In addition, the article described here raises further questions in context with the interaction of GPR30 and mineralocorticoid receptor. What does the disparity of the aldosterone concentration between extracellular signal-regulated kinase activation and myosin light chain phosphorylation mean? Are they mediated by the same signaling?

Disclosures

None.

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