Aldosterone Rapidly Induces Leukocyte Adhesion to Endothelial Cells: A New Link Between Aldosterone and Arteriosclerosis?

To the Editor:

Aldosterone is known to induce cardiovascular dysfunction, including fibrosis, inflammation, and endothelial dysfunction, as well as thrombosis formation.1 Clinical trials have shown aldosterone to be an independent predictor of increased mortality in patients with chronic heart failure,2 and high circulating plasma aldosterone levels predict the clinical outcome in patients after myocardial infarction.3 Mineralocorticoid receptor blockade proved to exert beneficial effects in clinical trials, such as the Randomised Aldactone Evaluation Study and the Eplerenone Post-Acute Myocardial Infarction Heart Failure Efficacy and Survival Study.4 Recent studies provided evidence for a role of aldosterone in the pathogenesis of arteriosclerosis.5 However, the exact mechanisms of adverse aldosterone actions in the cardiovascular system are largely unknown. Here, we aimed at elucidating rapid (60 minutes) aldosterone effects on interactions between endothelial cells and leukocytes.

We performed adhesion experiments using primary cultures of freshly isolated human endothelial cells from the umbilical cord vein (HUVECs) and polymorphonuclear leukocytes (PMNs).6 Adhesion of leukocytes is mediated by adhesion molecules such as intercellular adhesion molecule-1, vascular cell adhesion molecule-1 and e-selectin.7 Therefore, we assessed expression of these molecules by Western blot analysis and immunohistochemistry8 in isolated HUVECs and human umbilical artery endothelial cells.

Figure 1A shows stimulated adhesion of PMNs to a monolayer of HUVECs after incubation of endothelial cells with increasing aldosterone concentrations (1 to 100 nmol/L). The effect observed was concentration dependent, indicating specificity for aldosterone. Leukocyte adhesion reaches a maximum after 1 hour with no further increase (Figure 1B). Figure 1C shows representative light microscopic images of adhering leukocytes.
after treatment of HUVECs with 10 nmol/L of aldosterone for 60 minutes. Figure 2 shows that expression of adhesion molecules is upregulated after a 1-hour treatment of HUVECs (Figure 2A and 2B) and human umbilical artery endothelial cells (Figure 2C and 2D) with 10 nmol/L of aldosterone.

Exposure of HUVECs to aldosterone (10 to 100 nmol/L) induces adhesion of PMNs to the endothelial cells within 60 minutes, suggesting absence of de novo mineralocorticoid receptor–mediated protein synthesis. Aldosterone is known to exert rapid effects by interfering with peptide signaling cascades, such as extracellular signal-regulated kinase 1/2 mitogen-activated protein kinases,9 and evidence suggests that rapid aldosterone effects might play a role in cardiac dysfunction.10 Mitogen-activated protein kinase activation is known to occur within minutes after aldosterone exposure to endothelial cells.11 Our data demonstrate a cellular mechanism of aldosterone-mediated endothelial dysfunction and support the idea of a rapid signaling mechanism as being responsible for the aldosterone-mediated upregulation of adhesion molecules.

Nonhemodynamic cardiovascular effects of aldosterone result in fibrosis and inflammation. Future studies will have to address the possible receptor that mediates rapid aldosterone effects and also will have to critically evaluate their pathophysiological importance in vivo.

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**Disclosures**

None.

**References**

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