Vessels and Endothelium

12.16 Primary Aldosteronism and Endothelial Progenitor Cell Bioavailability

A. Verhovez (1), A. Zeoli (1), T.A. Williams (1), F. Morello (1), E. Saglio (1), A. Viola (1), F. Tosello (1), M.F. Brizzi (1), F. Veglio (1), P. Mulatero (1)

(1)Università di Torino, Torino, Italy

Introduction. Patients with primary aldosteronism (PA) experience more cardiovascular events than patients with essential hypertension matched for risk factor profile. Endothelial progenitor cells (EPC) represent a bone marrow-derived cell population implicated in vascular healing whose number correlates to the cardiovascular risk factor profile. Aldosterone has been reported to decrease EPC proliferation in rats.

Methods. We assessed (1) the growth characteristics of EPC from 6 PA patients and 6 normotensive controls matched for age, sex and body mass index (2) the growth characteristics of EPC treated with increasing doses of aldosterone. We assessed senescence and cell-cycle analysis of EPC from PA patients and normotensive controls and of aldosterone-treated EPC from healthy volunteers. As a positive control EPC derived from Type 2 diabetic patients were used.

Results. No difference was found in the senescence rate between EPC from PA patients ($72.4\% \pm 7.6$ senescent cells) and controls ($70.7\% \pm 8.4$, $p > 0.05$) while in diabetic patients was significantly higher (85.6 ± 6.5 , $p > 0.05$). No difference was also found in the cell-cycle distribution determined by FACS (controls: $75.2\% \pm 2.3$ cells in G0/G1 phase; PA: $73.5\% \pm 7.8$, $p > 0.05$, diabetic patients $89.5\% \pm 6.4$, $p < 0.05$). Furthermore, the number of EPC in PA patients was not significantly different from that in normotensive controls (45 ± 10 vs 42 ± 13 , $p > 0.05$; but it was lower in diabetic patients: 30 ± 8 , $p < 0.05$). Incubation of EPC with aldosterone did not modify their senescence rate (controls: $72.4\% \pm 8.9$ senescent cells; aldosterone 10 nmol/L: $70.9\% \pm 7.3$; aldosterone 100 nmol/L: $71.6\% \pm 9.2$, $p > 0.05$ for all comparisons) and cell-cycle distribution (controls: $73.3\% \pm 1.8$ cells in G0/G1 phase; aldosterone 10 nmol/L: $74.9\% \pm 2.4$; aldosterone 100 nmol/L: $75.4\% \pm 1.8$, $p > 0.05$ for all comparisons). No expression of the mineralocorticoid receptor (MR) transcript was found in EPC by RT-PCR analysis.

Conclusions. High aldosterone levels, both in PA patients and in vitro, exert no direct or indirect effect on EPC growth characteristics. While the lack of MR expression in EPC explains the absence of an effect by aldosterone in the in vitro experiments, the results of the in vivo experiments indicate that aldosterone acts neither directly on EPC nor indirectly in the bone marrow milieu or in the peripheral circulation to induce EPC dysfunction and reduced bioavailability.