IJAE
Vol. 121, n. 1 (Supplement): 19, 2016
ITALIAN JOURNAL OF ANATOMY AND EMBRYOLOGY

Gender differences in estrogenic compounds effect on human EPCs

Ilaria Campesi [1] - Giampiero Capobianco [2] - Salvatore Dessole [2] - Flavia Franconi [1,3] - Andrea Montella [4]

[1] Dipartimento di Scienze Biomediche, Università di Sassari, Sassari, Italia - [2] Dipartimento di Scienze Chirurgiche, Microchirurgiche e Mediche. Clinica Ginecologica e Ostetrica, Università di Sassari - AOU Sassari, Sassari, Italia - [3] Assessorato alle Politiche per la Persona della Basilicata, Potenza, Italia – [4] Dipartimento di Scienze Biomediche, Università di Sassari - AOU Sassari, Sassari, Italia

Endothelial dysfunction has been defined as an "integrated risk factor", and several gender difference have been reported in endothelial function. Several evidences suggest that endothelial progenitor cells (EPCs) are an important endogenous system that maintains integrity and vascular homeostasis. Their function is regulated by estrogens and estrogen receptors (ERs), but the effect of estrogenic compounds such as bisphenol A (BPA) and (R,R)-5,11-diethyl-5,6,11,12-tetrahydro-2,8-chrysenediol (THC) on human EPCs is unknown. BPA is used in plastic industry and BPA exposure is associated to abnormalities such as obesity, diabetes, disorders of the reproductive and immune systems, to endothelial dysfunction, and oxidative stress. This endocrine disruptor binds to ERα and ERβ with higher affinity for ERβ. THC is a specific agonist of ERα with a stronger ERβ antagonist activity. Therefore, the present work aimed to analyze if BPA and THC influence in a sex-specific manner the migration of human EPCs, an essential process in endothelial regeneration after vascular injury. EPCs were isolated from healthy adult men and women aged between 18 and 30 years, using a magnetic positive selection with the CD34 MicroBeads, a well-established marker of human progenitor cells. EPCs were also characterized for acetylated LDL Dil- (acLDL) and isothiocyanate (FITC)-conjugated with Ulex europaeus agglutinin I (lectin) uptake. The expression of ERα and ERβ was analysed by Western Blotting, while the migration assay was performed with the transwell chemotaxis assay. Male and female EPCs expressed both classical ERs: ERα was higher, but not significantly, in female cells, while ERβ was similarly expressed in both sexes. Male and female EPCs did not differ in basal migration. 17-β-estradiol (10^{-9} M e 10^{-10} M) significantly inhibited migration in female EPCs but not in male ones. Moreover, both 10^{-5} M THC and BPA (10^{-8} M) were able to bock migration only in female cells. Considering that BPA has a ERα and a prevalent ERβ agonist activity while THC has ERα agonistic activity and a prevalent ERβ antagonist activity, our data show that the effect on migration observed in female EPCs is mediated by ERα. Our data demonstrate that estrogenic compound have a sexual divergent effect on human EPCs, improving our knowledge on the gender differences observed in the pathophysiology of endothelial function.

Keywords

EPCs; gender; migration; estrogenic compounds.