IJAE
Vol. 119, n. 1 (Supplement): 33, 2014
ITALIAN JOURNAL OF ANATOMY AND EMBRYOLOGY

Human umbilical endothelial cells (HUVECs) and sex differences

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HUVECs are worldwide used to study the endothelial physiology and pathology that might be involved in sex and gender differences detected at the cardiovascular level. The present work characterised the phenotype of HUVECs in terms of morphology, proliferative and migratory capacity and in the gene expression of oestrogen and androgen receptors and nitric oxide synthase 3 (NOS3) to evaluated if they are sexually dimorphic. Moreover, autophagic process was analysed in male and female HUVECs (MHUVECs and FHUVECs), as autophagy is influenced by sex.

Umbilical cords were obtained from healthy, normal weight, male and female neonates born to healthy non-obese and non-smoking women. HUVECs morphology was analysed by electron microscopy, and their function was investigated by proliferation, viability, wound healing and chemotaxis assays. Real-time PCR was used to evaluate gene expression for oestrogen and androgen receptors and for NOS3, while the expression of the primary molecules involved in autophagic process [(Akt, the mammalian target of rapamycin (mTOR), beclin-1 and microtubule-associated protein 1 light chain 3 (LC3)] and NOS3 were analysed by western blotting.

FHUVECs showed significantly higher proliferation and migration rate, and NOS3 mRNA and protein expression than MHUVECs. Conversely, beclin-1 and the LC3-II/LC3-I ratio were higher in MHUVECs than in FHUVECs, indicating a higher autophagy in male cells as also indicated by ultrastructural analysis showing a build-up of autophagic vacuoles at different stages in MHUVECs. The expression of oestrogen and androgen receptor genes, the protein expression of Akt, mTOR, and cellular size and shape were not influenced by sex. Male and female neonates did not differ in body weight, but the weight of male babies was positively associated with the weight of the mother, suggesting that the weight of the mother may exert a different influence on male and female babies.

Our findings indicate that sex differences exist from prenatal life and are parameter-specific, suggesting that a better quality of the research on the endothelium in vitro can be obtained by analyzing HUVECs of both sexes as well as its translational value. Moreover, the sex differences observed in HUVECs could help the diseases of adulthood because endothelial dysfunction has a key role in cardiovascular diseases, diabetes mellitus, neurodegeneration and immune diseases.

Keywords

Sex differences, HUVECs, autophagy, birth weight.