



Session OR01 - Gynecology I

O-019 - Acute DEHP Exposure in Endometrial Epithelial Cells Does Not Phenocopy the Alterations Described in Endometriosis.

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Categories

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Abstract

Introduction: Some phenotypic alterations described in endometriosis, such as increased cell viability, immune response, invasive capacity, and altered steroid receptor expression, have been replicated on Ishikawa and primary endometrial stromal cells (ESC) following acute Di(2-ethylhexyl)phthalate (DEHP) exposure [Sung-Hoon et al. (2015), Cho et al. (2015)]. Yet, it remains unknown how DEHP exposure affects primary endometrial epithelial cells (EEC). We hypothesized that DEHP exposure *in vitro* could induce changes in the EEC that replicate phenotypic alterations observed in endometriosis.

Methods: Primary EEC were isolated by gravity sedimentation from endometrial biopsies collected from healthy oocyte donors recruited in the clinic IVI Valencia, the day of ovarian puncture (n=4). EEC were exposed to DEHP (0.1-10 μ M) or vehicle (0.002% DMSO) for 0, 24, 48, and 72 hours (h). We evaluated the number of viable cells at each time point using a cell proliferation assay (MTS, Promega). EEC exposed to DEHP (0.1-10 μ M) or vehicle (0.002% DMSO) for 48 h were analyzed for gene expression by qPCR (StepOnePlus Real-Time PCR System, Applied Biosystems) for the following targets: an inflammatory gene (*IL6*), an angiogenic gene (*VEGFA*), an endometrial morphogenic gene (*HOXA10*), five steroid receptors (*ER- α* , *ER- β* , *PR-T*, *PR-B*, *PGRMC1*) and two epigenetic modulators (*KDM1A* and *EZH2*), all previously described as altered in eutopic endometrium from endometriosis patients.

Results: We did not find any statistically significant difference in viability of EEC or in expression of any of the ten target genes selected post-acute exposure to DEHP (0.1-10 μ M) (n=4). However, *EZH2* expression trended toward a dose-dependent increase at DEHP doses 0.1-10 μ M and *HOXA10* expression trended toward a decrease at DEHP doses 0.1-1 μ M, both similar to that described in endometriosis.

Conclusion: Our observations suggest that *in vitro* acute exposure (0-48 h) of EEC to DEHP (0.1-10 μ M) does not trigger the phenotypic alterations described in the eutopic endometrium of women with endometriosis. We cannot exclude that such alterations might occur at later timepoints or following longer exposure. Funded by a grant from the IVI Foundation, Miguel Servet Contract (CP013/0450) and ISCIII FIS project (PI17/00931).