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— From Innovation to Impact —

Session PO1-11a - Reproductive Biology I

T-241 - Copper and Lead, Two Inorganic Metalloestrogens, Disturb Reproductive Features of Primary Endometrial Stromal (ESC) and Epithelial Cells (EEC).

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Categories
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Abstract

Introduction: Copper (Cu) and lead (Pb) are metalloestrogens that invoke an estrogenic response in cultured MCF7 breast cancer cells (Martin et al., 2003). Cu also affects decidualization in immortalized human endometrial stromal cells (ESC) (Ying Li et al., 2016). However, the effect of Cu and Pb on primary ESC and endometrial epithelial cells (EEC) is not well understood. We analyzed the effects of ***in vitro*** exposure to Cu and Pb on ESC and EEC viability, steroid receptor expression, migration, and decidualization capacity.

Methods: Primary ESC and EEC were isolated from endometrial biopsies collected from oocyte donors on the day of ovarian puncture (n=7). ESC (n=4) and EEC (n=4) were exposed to Cu (0-200 µM) or Pb (0-500 µM) for 96 hours (h) (ESC) or 48 h (EEC) and checked for viability using colorimetric MTS assay (Promega). For the decidualization study, ESC (n=3) were pre-treated with Cu (0 and 50 µM) or Pb (0, 30, and 100 µM) for 24 h. Decidualization was then induced with P4+E2 for 8 days. Decidualization was assessed by prolactin (PRL) measurement in culture media by ELISA (Abnova). mRNA expression of steroid receptors (***PR*** & ***ER-α***) was analyzed by qPCR (Applied Biosystems). For the wound-healing assay, confluent EEC (n=3) were scratched with a tip and immediately exposed to Cu (0, 50, and 100 µM) or Pb (0, 30, and 100 µM) for 72 h. Wound width was measured every 24 h after scratching.

Results: Cell viability was significantly reduced ($p<0.01$) in EEC and ESC exposed to Cu (100-200 µM) at 48 h and 96 h vs. controls. EEC underwent a significant increase ($p<0.05$) in viability at 30, 100, and 500 µM Pb. Furthermore, Cu had a cytotoxic effect at 200 µM, while Pb appeared to promote proliferation. PRL secretion was significantly decreased ($p<0.001$) after 8 days of decidualization at each dose of Cu and Pb vs. controls. ***PR*** and ***ER-α*** mRNA expression were lower in decidual cells exposed to 30 and 100 µM of Pb and 50 µM of Cu vs. control. Finally, migration capacity was significantly reduced ($p<0.05$) vs. controls when EEC were exposed to 50 and 100 µM of Cu.

Conclusion: Cu and Pb could act as reproductive disruptors, reducing steroid receptors expression and inhibiting decidualization in ESC. Furthermore, Cu could also reduce the regenerative capacity of EEC.