

Effects of multiple exposure of endocrine disrupting chemicals on atherosclerosis

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Background/Aims: This study aim to identify the association between multiple exposure of EDCs and atherosclerosis using vascular smooth muscle cell (VSMC)

Methods: We conduct in vitro experiments with VSMCs collected from thoracic aorta of male Otsuka Long-Evans Tokushima Fatty rats. We tested the proliferation, migration, apoptosis and the production of reactive oxygen species (ROS) according to single low exposure of BPA and combined exposure to BPA and other endocrine disrupting chemicals (EDC) including 1,1-Dichloro-2,2-bis(4-chlorophenyl)ethane (DDE), Bis(2-ethylhexyl) phthalate (DEHP), Benzophenone 3 and Ethylhexyl methoxycinnamate (EHMC)

Results: BPA induced significant increase in MAPK pathway (pMEK1/2, p-value <0.001; pERK1/2, p-value 0.014). In wound healing assay, the percentage of migrating cells increased significantly (p-value 0.004), while expression of pBMK-1 (p-value <0.001) and pMMP-2 (p-value 0.018) also increased significantly. In the apoptotic signaling pathway, the expression of pBad (p-value 0.021) and Bax (p-value <0.001) increased and Bcl-2 (p-value <0.001) decreased significantly. BPA showed significant increase in ROS generation (p-value: 0.039). In the experiment with EDC mixture, VSMC proliferation increased significantly (p-value 0.025). EDC mixture induced significant increase in MAPK pathway (pMEK1/2, p-value 0.002; pERK 1/2 p value 0.003) and PI3K/AKT pathway (pPI3K, p-value 0.003; pAKT, p-value 0.023). In wound healing assay, the percentage of migrating cells increased significantly (p-value 0.005), while expression of pBMK-1 (p-value 0.016) and pMMP-2 (p-value <0.001) also increased significantly. In the apoptotic signaling pathway, the expression of pBad (p-value 0.001) and Bax (p-value 0.013) increased and Bcl-2 (p-value 0.001) decreased significantly. BPA showed significant increase in ROS generation (p-value < 0.001).

Conclusions: The study proved the direct effect of BPA on VSMCs from cell proliferation, migration, apoptosis and ROS generation. Furthermore, its mixture with other EDCs showed more increase of those effect on VSMC than single exposure of BPA did.