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Association between Diethyl Phthalate (DEP) exposure and hypertension in pregnancy: an *ex vivo* vascular approach

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Abstract

Background: Hypertensive disorders in pregnancy are one of the leading causes of gestational morbidity and mortality [1]. Several risk factors have already been identified, such as a sedentary lifestyle, advanced age, alcohol and tobacco consumption, and familial predisposition, but a new one is gaining prominence due to its high presence in our daily lives, which is exposure to environmental contaminants. Being widely used in the plastic industry, phthalates are one of these environmental contaminants, due to their ubiquitousness and endocrine disrupting properties [2,3]. Besides, phthalates have been associated with impaired health, and a link with pregnancy hypertension has already been suggested in some epidemiological studies [4-6]. **Objective:** To analyze the connection between diethyl phthalate (DEP) exposure and hypertension in pregnancy and its vascular impacts. Methods: Human umbilical arteries (HUA) from normotensive and hypertensive pregnant women were collected, and DEP's non-genomic (within minutes) and genomic (24h exposure) effects on vascular reactivity were analyzed, through the organ bath technique. A range of DEP concentrations was analyzed over the response of three different vasocontractile agents (serotonin, histamine, and KCl) as well as the contribution of cyclic guanosine monophosphate (cGMP) and Ca^{2+} channels pathways. **Results:** The non-genomic effects show that DEP leads to an endothelium-independent vasorelaxation by interfering with serotonin and histamine receptors. After 24h exposure, the results show that the vasorelaxant effect of DEP seems to occur through the NO/sGC/cGMP/PKG signaling pathway, and to interfere with the L-type Ca^{2+} channels. **Conclusions:** The vascular effects induced by DEP in normotensive HUA are similar those from hypertensive pregnancies, suggesting that the development of hypertension in pregnancy may be a consequence of exposure to DEP.

Keywords: personal-care products; diethyl phthalate; hypertensive disorders in pregnancy; human umbilical arteries; vasorelaxation

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