

ESTROGEN RECEPTOR ALPHA (ER- α) AND CYTOCHROME P450 17 (CYP17) GENOTYPES, AND PLASTICIZER EXPOSURE ON THE OCCURRENCE OF LEIOMYOMA

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Background and Aims: Evidence has shown that polymorphisms of various genes known to be involved in estrogen biosynthesis and function including CYP17, CYP1A1, estrogen receptor-alpha and -beta, are associated with estrogen dependent diseases. Phthalates are considered estrogenic endocrine disruptors and may act as a risk factor for estrogen dependent diseases (EDDs) in recent studies. We aim to assess the gene-environmental interactions on EDDs.

Methods: We recruited 44 patients with endometriosis or adenomyosis, 36 patients with leiomyoma and 68 healthy controls from a medical center in Taiwan between 2005 and 2007. Urine samples were collected and analyzed for seven phthalate metabolites using liquid chromatography tandem mass spectrometry. Peripheral lymphocytes were used for DNA extraction to determine the genotype of CYP17, CYP 1A1, ER- α and ER- β .

Results: Patients with leiomyoma had significantly higher levels of total urinary mono-ethylhexyl phthalate (\bullet MEHP; 52.1 vs. 29.6 \bullet g/g creatinine (\bullet g/g-c)), mono-*n*-butyl phthalate (MnBP; 75.4 vs. 51.3 \bullet g/g-c) and monoethyl phthalate (MEP; 103.7 vs. 59.3 \bullet g/g-c) than the controls, whereas patients with endometriosis or adenomyosis only had an increased level of urinary MnBP. Subjects who carried the ER- α W allele and CYP17 A2 allele showed a significantly increased risk for leiomyoma (OR = 9.98, 95%CI: 1.30-76.52, $p=0.027$) after adjustment for age, GSTM1, MEHP and cigarette smoking, as compared to those with ER- α and CYP17 wild type. We suggested that both CYP17 and ER- α polymorphism may be a modifier for phthalate exposure in the development of leiomyoma.