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Abstract

Introduction: Exposure to certain heavy metals, called metalloestrogens, can interfere with endocrine function. Thus, heavily hormonally-regulated processes such as menarche and menopause are particularly susceptible to effects from long-term exposure to these agents. We aimed to identify the relationship between circulating heavy metals (cadmium and lead) and the age of menarche and menopause as well as women's reproductive lifespan.

Methods: We used data from the National Health and Nutrition Examination Survey (NHANES), 2005-2014 to select a population of post-menopausal women without ovarectomy or hysterectomy before menopause onset and with data available for all our outcomes of interest (n = 2681). We assessed cadmium and lead concentrations in whole blood along with self-reported age of menarche and menopause. Reproductive lifespan was defined as the time between menarche and menopause. We first defined the baseline characteristics of participants by categories of age of menarche (premature [<10 years], normal [10-14 years], and delayed [>14 years]) and age of menopause (premature [<48 years], normal [48-54 years], and delayed [>54 years]) or by cadmium and lead tertiles. We then used logistic regression to estimate 95% confidence intervals (CIs), comparing the 4 highest quintiles of blood cadmium and lead with the lowest quintile and adjusting by 3 models of potential confounders (model 1: sociodemographic factors; model 2: model 1 and toxic habits [smoke and alcohol consumption]; model 3: model 2 and the other heavy metal blood level).

Results: The relative risk after multivariable adjustment (95% CIs lowest vs highest quintile) for reproductive life were 1.40 (95% CI: 0.24, 2.55) for blood cadmium and 0.54 (-0.29, 1.38) for blood lead. Age at menopause exhibited the same trend for blood cadmium 1.42 (0.30, 2.54) and lead 0.41 (-0.41, 1.22). No association was found between cadmium/lead blood levels and age of menarche of the postmenopausal participants.

Conclusion: Delayed age of menopause was associated with higher blood levels of metalloestrogens (cadmium and lead). These results must be interpreted with caution, given the potential for unmeasured confounders such as bone metabolism and parity status. Funded by a grant from the IVI Foundation and Miguel Servet Contract (CP013/0450)