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Circulating 2-Hydroxy- and 16 α -Hydroxy Estrone Levels and Risk of Breast Cancer among Postmenopausal Women

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Circulating estrogens are associated with breast cancer risk in postmenopausal women. Given that estrogen metabolites are potentially both mitogenic and genotoxic, it is possible that plasma levels of estrogen metabolites are related to breast cancer risk. We conducted a prospective, nested case-control study within the Nurses' Health Study. Blood samples, collected in 1989 to 1990, were assayed for 2-OH and 16 α -OH estrone among 340 cases and 677 matched controls not taking postmenopausal hormones. Multivariate relative risks (RR) and 95% confidence intervals (95% CI) were calculated by conditional logistic regression, adjusting for breast cancer risk factors. Neither 2-OH nor 16 α -OH estrone concentrations were significantly associated with breast cancer risk overall (top versus bottom quartile: RR, 1.19; 95% CI, 0.80-1.79; $P_{\text{trend}} = 0.40$ for 2-OH estrone and RR, 1.04; 95% CI, 0.71-1.53; $P_{\text{trend}} = 0.81$ for 16 α -OH estrone). The ratio between the two metabolites (2-OH:16 α -OH estrone) was similarly unrelated to risk overall (1.30; 95% CI, 0.87-1.95; $P_{\text{trend}} = 0.35$). Although no associations were detected among women with estrogen receptor (ER)-positive/progesterone receptor (PR)-positive tumors, significant positive associations were observed for 2-OH estrone and the 2-OH:16 α -OH estrone ratio among women with ER-negative/PR-negative tumors (RR, 3.65; 95% CI, 1.23-10.81; $P_{\text{trend}} = 0.01$; $P_{\text{heterogeneity}} = 0.02$ for 2-OH estrone; RR, 3.70; 95% CI, 1.24-11.09; $P_{\text{trend}} = 0.004$; $P_{\text{heterogeneity}} = 0.005$ for 2-OH:16 α -OH estrone). These data do not support the hypothesized inverse associations with 2-OH estrone and the 2-OH:16 α -OH estrone ratio or the hypothesized positive association with 16 α -OH estrone. The significant positive associations with 2-OH estrone and the 2-OH:16-OH estrone ratio among women with ER-negative/PR-negative tumors needs to be replicated in future studies. (*Cancer Epidemiol Biomarkers Prev* 2008;17(8):2029-35)

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