

Prenatal exposure to bisphenol A promotes angiogenesis and alters estrogen receptor alpha-mediated responses in the mammary gland of cycling rats

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Prenatal exposure to bisphenol A (BPA) disturbs mammary gland histoarchitecture and increases the carcinogenic susceptibility to chemical challenges administered long after BPA exposure. Our aim was to assess the effect of prenatal BPA exposure on mammary gland angiogenesis and steroid hormone signaling pathways in virgin cycling rats. Pregnant Wistar rats were exposed to either 25 or 250 µg/kg bw/day (25 and 250 BPA, respectively) or to vehicle. Female offspring were autopsied on postnatal day (PND) 50 or 110. Ovarian steroid serum levels, proportion of hyperplastic ducts, the expression of steroid receptors and their co-regulators in the mammary gland, and angiogenesis were evaluated. At PND 50, all BPA-treated animals had lower serum levels of progesterone, while estradiol levels remained unchanged. At PND 110, animals exposed to 25 BPA exhibited an increased frequency of hyperplastic ducts. Additionally, samples from animals exposed to 250 BPA showed a trend toward increased presence of hyperplastic ducts. The higher dose of BPA increased estrogen receptor alpha and decreased Steroid Receptor Coactivator-3 expression at PND 50 and PND 110. Silencing Mediator of Retinoic Acid and Thyroid Hormone Receptor (SMRT) protein levels were similar among groups at PND 50, whereas at PND 110, animals exposed to 250 BPA showed a lower SMRT expression. Interestingly, in the control and 25 BPA groups, SMRT increased from PND 50 to PND 110. At PND 50, an increased vascular area associated with higher Vascular Endothelial Growth Factor (VEGF) expression was observed in

the 250 BPA-treated rats. At PND 110, the vascular area was still increased, but VEGF expression was similar to that of control rats. The present results demonstrate that prenatal exposure to BPA alters the endocrine environment of the mammary gland and its angiogenic processes. Increased angiogenesis and altered steroid hormone signals could explain the higher frequency of pre-neoplastic lesions found later in life in treated rats. (This study was supported by grants from the Argentine National Agency for the Promotion of Science and Technology and from Universidad Nacional del Litoral).

Poster Category: Recent scientific data