

Abstract P3-09-03: Combined effects of soy isoflavones and a high fat diet on the mammary gland in an animal model of diet-induced obesity

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Abstract

Scope: Obesity is a major risk factor for the development of breast cancer whereas isoflavone (ISO) exposure is discussed to reduce this risk. Aim of this study was to investigate effects of dietary soy ISO intake on proliferation and estrogenicity of ISO in the mammary gland of obese female Wistar rats.

Methods: Female Wistar rats (5 – 7 rats / group) grew up on low fat ISO-depleted diet (LF IDD) or ISO-rich diet enriched with a soy based commercial extract (LF IRD; ISO: 467 mg /kg diet). Starting postnatal day 83, ovariectomized (OVX) and intact animals received high fat diet for 12 weeks to induce obesity in the absence (HF IDD) or presence of ISO (HF IRD, ISO: 431 mg / kg diet). A special diet switch group (HF IRD switch OVX), grew up on LF IDD but switched to HF IRD after ovariectomy. This mimics the short term exposure to ISO in postmenopausal Western women who take ISO supplements. Two groups receiving LF diet either with or without ISO (LF IRD, LF IDD) lifelong served as control. From ablactation until the end of the experiment body weight and food consumption were monitored twice a week. After 12 weeks of HF diet animals were sacrificed. Body weight, visceral fat mass, and serum leptin were measured, and breast tissue was excised. Protein expression of proliferating cell nuclear antigen (PCNA) and progesterone receptor (PR) in breast tissue was analyzed by both immunohistochemistry (IHC) and Western Blot as markers for proliferation and estrogenicity of ISO, respectively.

Results: Analysis of ISO plasma levels revealed 1400 nM in LF IRD group and 300 – 700 nM in HF IRD groups. HF diet increased body weight, visceral fat mass and serum leptin levels compared to LF diet. In the mammary gland HF increased expression of proliferation marker PCNA and PR as compared to LF groups. Lifelong but not short term (HF IRD switch OVX) ISO exposure reduced body weight, visceral fat mass and leptin levels in HF OVX rats. In the mammary gland lifelong ISO exposure reduced PCNA expression in both LF and HF intact animals whereas in HF OVX animals lifelong ISO exposure increased PCNA expression compared to short term ISO exposure. PR expression increased in HF IRD OVX compared to HF IDD OVX.

Conclusion: The ISO plasma levels of the rats are comparable to the average ISO plasma levels as found in Asian population. Our results show that lifelong ISO intake reduces the risk to develop obesity in female rats. In the mammary gland lifelong ISO exposure decreases cell proliferation and shows estrogenicity by increasing PR expression. Effects of short term ISO exposure are less strong compared to lifelong ISO exposure. This supports the hypothesis that only lifelong but not short term ISO exposure can reduce the risk to develop breast cancer.

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