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Soy supplementation and role of equol production capability in postmenopausal women using tibolone: effects on cardiovascular risk markers

Academic dissertation

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ABSTRACT

Tibolone, a synthetic steroid, is effective in the treatment of postmenopausal symptoms. Its cardiovascular safety profile has been questioned, because tibolone reduces the levels of high-density lipoprotein (HDL) cholesterol. Soy-derived isoflavones may offer health benefits, particularly as regards lipids and also other cardiovascular disease (CVD) risk factors. The soy-isoflavone metabolite equol is thought to be the key as regards soy-related beneficial effects. We studied the effects of soy supplementation on various CVD risk factors in postmenopausal monkeys and postmenopausal women using tibolone. In addition, the impact of equol production capability was studied.

A total of 18 monkeys received casein/lactalbumin (C/L) (placebo), tibolone, soy (a woman's equivalent dose of 138 mg of isoflavones), or soy with tibolone in a randomized order for 14 weeks' periods, and there was a 4-week washout (C/L) in between treatments. Postmenopausal women using tibolone (N=110) were screened by means of a one-week soy challenge to find 20 women with equol production capability (4-fold elevation from baseline equol level) and 20 control women, and treated in a randomized cross-over trial with a soy powder (52 g of soy protein

containing 112 mg of isoflavones) or placebo for 8 weeks. Before and after the treatments lipids and lipoproteins were assessed in both monkeys and women. In addition, blood pressure, arterial stiffness, endothelial function, sex steroids, sex hormone-binding globulin (SHBG), and vascular inflammation markers were assessed.

A 14% increase in plasma low-density lipoprotein (LDL) + very low-density lipoprotein (VLDL) cholesterol was observed in tibolone-treated monkeys vs. placebo. Soy treatment resulted in a 18% decrease in LDL+VLDL cholesterol, and concomitant supplementation with tibolone did not negate the LDL+VLDL cholesterol-lowering effect of soy. A 30% increase in HDL cholesterol was observed in monkeys fed with soy, whereas HDL cholesterol levels were reduced (48%) after tibolone. Interestingly, Soy+Tibolone diet conserved HDL cholesterol levels. Tibolone alone increased the total cholesterol (TC):HDL cholesterol ratio, whereas it was reduced with Soy or Soy+Tibolone.

In postmenopausal women using tibolone, reductions in the levels of total cholesterol and LDL cholesterol were seen after soy supplementation compared with placebo, but there was no effect on HDL cholesterol, blood pressure, arterial stiffness or endothelial function. Soy supplementation decreased the levels of estrone in equol producers, and those of testosterone in the entire study population. No changes were seen in the levels of androstenedione, dehydroepiandrosterone sulfate, or SHBG. The levels of vascular cell adhesion molecule-1 increased, and platelet-selectin decreased after soy treatment, whereas C-reactive protein and intercellular adhesion molecule-1 remained unchanged. At baseline and unrelated to soy treatment, equol producers had lower systolic, diastolic and mean arterial pressures, less arterial stiffness and better endothelial function than non-producers.

To conclude, soy supplementation reversed the tibolone-induced fall in HDL cholesterol in postmenopausal monkeys, but this effect was not seen in women taking tibolone. Equol production capability was associated with beneficial cardiovascular changes and thus, this characteristic may offer cardiovascular benefits, at least in women using tibolone.

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