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Physiological levels of estradiol stimulate plasma high density lipoprotein2 cholesterol levels in normal men.

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Abstract

Premenopausal women have a lower risk of coronary artery disease than men or postmenopausal women; estrogens are thought to contribute to this lower risk. Administration of exogenous estrogen to post-menopausal women increases plasma high density lipoprotein (HDL) cholesterol and may reduce mortality from coronary disease in users. Although many investigations have examined the roles of estrogen in the regulation of lipoproteins in women, little attention has been directed to estrogen regulation of lipids in men. We designed a paradigm to study the role of physiological levels of estradiol (E2) on plasma lipoproteins in healthy men. We used a GnRH antagonist, Nal-Glu, to suppress endogenous steroid hormones in healthy men. We then administered testosterone (T) enanthate (100 mg, im, weekly) to restore T levels to the baseline range, and we administered an aromatase inhibitor, testolactone (Teslac), to prevent the normal conversion of T to E2, thereby producing a selective estrogen deficiency state in normal young men. As controls, we administered Nal-Glu and T along with placebo Teslac to a separate group of men; a third group of men received all placebo medications. We found that in men who received Nal-Glu plus T plus Teslac, E2 levels were profoundly suppressed during treatment, whereas T levels remained in the baseline range. Plasma HDL cholesterol, particularly, the HDL2 fraction, decreased significantly in response to the low serum E2 level. Plasma apoprotein-AI levels also decreased significantly. Plasma LDL and triglyceride levels did not change. All hormone and lipoprotein parameters returned to baseline within 4 weeks after treatment ended. In men who received Nal-Glu plus T, plasma HDL and apoprotein-AI decreased, but these decreases did not achieve statistical significance. Only a small decrease in HDL2 cholesterol was seen in these men. There were no hormonal or lipid changes in the placebo group. We conclude that in men, physiological levels of E2 are important in maintaining plasma levels of HDL cholesterol, especially the HDL2 fraction. These observations suggest that estrogen, in the amount normally produced in men, may offer some degree of protection against cardiovascular disease in males, as they do in women.