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Dietary genistein influences function of mouse aorta

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Cardiovascular disease is the leading cause of death for men and postmenopausal women in the United States. Estrogen is thought to be cardioprotective. An important action of estrogen is increasing endothelial-dependent vasodilation of coronary arteries. Because of their estrogen-like components and activities, phytoestrogens, especially isoflavones such as genistein found in high concentrations in soy products, are being studied as a potential means to prevent cardiovascular disease and as an alternative to estrogen replacement therapy. In the current study we examined the effects of high dietary genistein on vascular function of mice. Since genistein is considered estrogenic, we hypothesized that genistein also would enhance vasodilation. Mice were divided into three diet groups: standard fed (200 mg genistein), high genistein (600 mg), and genistein-free (0 mg). After being on their respective diets for at least one month, the mice were sacrificed, thoracic aortas were isolated, cleaned of surrounding fat and connective tissue, and then cut into rings to measure contractile capacity. Receptor independent contractility was measured by adding increasing doses of potassium chloride (KCl). Both males and females fed 600 mg genistein showed significantly greater force of contractions at all doses of KCl above 30mM compared to other groups. The 0 mg group exhibited the least amount of tension for all KCl doses. Receptor dependent contractility was measured following increasing concentrations of norepinephrine (NE) in the presence and absence of NG-nitro-L-arginine methyl ester (L-NAME), a nitric oxide synthase (NOS) inhibitor. In the absence of L-NAME contractile responses to NE followed the KCl pattern for diet groups except for the 600 mg male group which was similar to the standard fed males. Therefore, the NE curves were normalized to the maximal KCl force. Normalization of NE to KCl indicated NE responses were similar for all groups except 600 mg males. To evaluate whether endothelial vasodilators alter contractile force mediated by NE, data were collected in the presence of L-NAME. The NE contractile responses with L-NAME were significantly greater than contractility without L-NAME for all groups. NOS contribution to vasodilation was significantly less in males compared to females. In females the contribution of NOS appeared greatest in the 600 mg group compared to other groups. These results show that vasodilation capacity is increased with high genistein (600 mg) diets with females, but not males. Surprisingly genistein significantly increased contractile force to KCl. Possible mechanisms that may underlie genistein effects on KCl contractions include increased L-type calcium currents and/or smooth muscle hypertrophy/hyperplasia.

