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Cardiovascular Effects of Raloxifene Hydrochloride

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ABSTRACT

Raloxifene hydrochloride binds to the estrogen receptor and shows tissue-selective effects; thus, it belongs to a class of drugs recently described as *selective estrogen receptor modulators* (SERMs). Tissue selectivity of raloxifene may be achieved through several mechanisms: the ligand structure, interaction of the ligand with different receptor subtypes in various tissues, and intracellular events after ligand binding. Raloxifene has estrogen-agonist effects on bone and lipids and estrogen antagonist effects on the breast and uterus. In addition to its well established effects on osteoporosis, recent preclinical and clinical findings suggest that raloxifene also possesses beneficial effects on the cardiovascular system. These findings indicated that raloxifene may have cardioprotective properties without an increased risk of cancer or other side effects. Raloxifene has been shown to reduce total and low-density lipoprotein cholesterol concentrations in plasma, an effect similar to that produced by estrogens. Unlike estrogens, however, raloxifene does not increase high-density lipoprotein cholesterol and triglyceride levels in plasma. Endothelium is thought to play an important role in the genesis of atherosclerosis. Several lines of evidence suggest that an intervention with endothelial function might influence the progression of coronary disease and the incidence of cardiovascular events. Raloxifene increases the nitric oxide/endothelin-1 ratio, and improves endothelium-dependent vasomotion in post-menopausal women to the same extent as estrogens. Furthermore, in two randomized trials on post-menopausal women raloxifene reduced homocysteine levels, another independent risk factor for the development of cardiovascular disease. Although estrogens remain the drugs of choice in the hormonal therapy of most postmenopausal women, raloxifene may represent and alternative in women who are at risk of coronary artery disease.