ISGE
GYNECOLOGICAL ENDOCRINOLOGY
THE 18TH WORLD CONGRESS
7-10 MARCH 2018 FLORENCE, ITALY

HRT for primary prevention of CHD

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Various routes of administration exist for hormone replacement therapy (HRT), such as oral, transdermal and subcutaneous, and their effects on metabolic risk factors for coronary heart disease (CHD) can differ. Oral estrogen lowers total cholesterol, LDL cholesterol and lipoprotein (a), and increases HDL cholesterol, whereas transdermal estradiol has a lesser effect. Oral estrogen improves the clearance of the atherogenic post-prandial lipid remnants. Oral estrogen increases triglyceride concentrations, although estradiol has a lesser effect than conjugated equine estrogens. Transdermal estradiol lowers triglyceride concentrations. Oral estradiol may improve glucose tolerance by increasing insulin sensitivity (reducing insulin resistance), whereas transdermal estradiol has a lesser effect. Progestogen addition impacts many metabolic effects. Androgenic progestogens impede the increases in HDL cholesterol and in insulin sensitivity, whereas the non-androgenic oral progesterone and dydrogesterone have no such adverse effects. Direct arterial effects of estrogens are important. Estradiol has beneficial effects on vascular endothelial function and its markers. Estradiol reduces angiotensin-converting enzyme (ACE) activity, another benefit. Substantial evidence has now established that HRT may prevent CHD. Many observational studies have demonstrated the association between postmenopausal HRT use and a reduction in CHD. The timing of initiation of HRT appears important. Evidence from both animal and human studies shows that the greatest beneficial effects of HRT on atheroma progression are seen when therapy is initiated fairly close to the menopause. Similarly, the reduction in coronary events is seen with HRT initiation within 10 years of the onset of menopause or below age 60 years. Meta-analyses of randomised clinical trials have clearly shown this. However, the apparent lack of benefit from HRT initiated above age 60 years may simply reflect the use of inappropriately high doses of estrogen given to these women, leading to adverse effects on coagulation activation and vascular remodelling. It is possible that much lower estrogen doses at initiation of therapy in these women might avoid this. The addition of unfavourable progestogens, such as medroxyprogesterone acetate, may also reduce estrogenic benefit. Thus, the type and dose of hormones used and the timing of the initiation in relation to the menopause may be critical for maximising CHD benefit.

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