

Metabolic impact of progestogens

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Progestogens given as a component of hormone replacement therapy (HRT) have their main metabolic impact on risk factors for coronary heart disease (CHD). There is an increasing abundance of evidence that HRT may prevent CHD providing it is administered in an appropriate manner. The timing of the intervention with HRT in relation to menopause onset is important, with the greatest benefits for CHD prevention being seen in those women initiating treatment in the early postmenopause. The selection of an appropriate dose of hormones according to the age of the patient is paramount at initiation of therapy. The choice of hormones is also important as different types have differing metabolic effects that impact on CHD risk. Both conjugated equine estrogens (CEE) and estradiol 17 β have certain positive metabolic and vascular effects, but the choice of progestogen is important. Estrogen has largely favourable effects on lipids and lipoproteins in a dose-dependent manner. There is a reduction in LDL cholesterol which is not influenced by progestogen addition. A beneficial increase in HDL cholesterol with estrogen may be blunted by the addition of progestogens with androgenic properties such as norgestrel or medroxyprogesterone acetate (MPA), although these progestogens may also reduce the rise in triglycerides induced by oral, but not transdermal, estrogen. These effects are not modified by the addition of the non-androgenic progestogens, micronized progesterone and dydrogesterone. Similarly, the improvement in insulin sensitivity seen with oestradiol, but to a lesser extent with CEE, is impeded by androgenic, but not by non-androgenic, progestogens. Androgenic progestogens have adverse vascular effects, whereas non-androgenic progestogens do not reduce the beneficial effects of estrogens. The Women's Health Initiative (WHI) demonstrated an eventual reduction in CHD events in women initiating CEE below age 60 years but this effect was not seen when combined with MPA. Thus, to maximise cardiovascular benefit from HRT, attention must be paid to the type and dose of hormones used. It would seem prudent to choose non-androgenic progestogens in HRT in this respect.

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