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Invited Editorial

Menopausal hormone therapy for women with obesity in the era of COVID-19

Obesity represents the condition of excessive body fat accumulation. According to the World Health Organization (WHO), obesity rates have almost been tripled since the 1970s. It is estimated that over 1.9 billion adults (39%) worldwide are overweight, of whom 650 million are obese (13%) [1]. The problem is especially important in the western world and affects particularly postmenopausal women. Indeed, approximately 50% of the latter are overweight, of whom 25% are obese [2–4]. Obesity often leads to other morbidities, such as type 2 diabetes mellitus (T2DM), dyslipidaemia, and hypertension; additionally, it increases the risk of gynaecological malignancies, cardiovascular disease (CVD), thrombosis, osteoarthritis and musculoskeletal disease [1–4].

Vasomotor symptoms (VMS) are generally more common in obese women than in normal-weight women. In the Study of Women's Health Across the Nation (SWAN), the likelihood of increased flushing was 1.27 times higher for any standard deviation (SD) increase in body fat percentage [5]. The women who gain weight during the transition to menopause are prone to develop VMS [2–5]. Menopausal hormone therapy (MHT), including tibolone and the combination of conjugated equine estrogens and bazedoxifene (CE/BZA), is the most effective treatment for VMS associated with menopause at any age. However, benefits are more likely to outweigh risks if the treatment is initiated for symptomatic women before the age of 60 years or within 10 years after menopause [6].

Specific caution is required for obese women because of their increased risk of thromboembolic disease. Obese women in the placebo arm of the Women's Health Initiative (WHI) study presented a 2.9-fold greater risk of venous thrombosis compared with normal-weight women [7]. This risk increases with age, body mass index (BMI) and the presence of thrombotic mutations [2–4]. In the era of COVID-19, the illness that is caused by the infection with the new coronavirus SARS-CoV-2, a new thrombotic risk factor has been added to this list. COVID-19 is associated with a systemic inflammatory response, often accompanied by activation of coagulation, especially in those with clinical disease. This favours the appearance of thrombotic events and may produce various coagulopathies [8].

Globally, the proportion of men and women who have tested positive for SARS-CoV-2 is comparable. However, men are about 60% more likely to develop severe illness or die from complications. It is not clear whether this is due to biological differences between the two genders, differences in behavioural habits, or differences in the rates of comorbidities [9]. People with obesity have low-grade inflammation and present comorbidities that adversely affect the outcomes of COVID-19. Early observations revealed that many patients, especially those who died from COVID-19, were obese. Indeed, obesity, especially when accompanied by T2DM, CVD or other physical, mental, and/or functional complications, has been persistently shown to be a predictor of severe COVID-19 illness and all-cause mortality [10,11].

COVID-19 is likely to remain a problem for many months or even years until effective preventive or therapeutic strategies are developed. Since obesity and other comorbidities cannot be treated within a few months, the least the physicians can do is to be aware of such associations, and aim to provide the best holistic care possible. This approach should be applied for women taking or requesting MHT. Oral MHT increases the risk of thromboembolic disease. However, the risk associated with transdermal MHT given at standard therapeutic doses is no greater than the baseline population risk [12]. Tibolone therapy carries a lower risk of thromboembolic disease, but it has been associated with bodyweight gain [2–4]. Low-dose vaginal oestrogens have not been associated with alterations in coagulation factors or increased thromboembolic risk [6,8].

Given the risks but also the beneficial effects of MHT on metabolic parameters, a personalized approach should be applied for the use of MHT in postmenopausal women with obesity. As a general principle, the lowest effective dose of oestrogens [0.3–0.4 mg conjugated equine oestrogens (CEE) or 0.5–1 mg oestradiol orally daily or 25–50 μg oestradiol transdermally] should be used. The transdermal route should be preferred due to the decreased risk of thromboembolic disease. The use of a metabolically neutral progestogen, such as natural progesterone, dydrogesterone or transdermal norethisterone, is recommended [2–4].

For women with confirmed or even suspected COVID-19, any type of systemic MHT should be stopped for the whole period of isolation or hospitalization. For hospitalized patients or those with reduced mobility at home, the use of low molecular weight heparin (LMWH) is recommended for a minimum of one week after hospital discharge or until full mobilization. The pre-COVID-19 MHT regimen should be recommenced only after full recovery and restoration of complete mobility, and it is advisable to consider changing to transdermal therapy [8]. In the era of COVID-19, telephone, video and online consultations are preferred and can be used to discuss menopause and MHT to reduce the risk of infection. In this era of the "new normal", health professionals should always weigh up the benefits and risks of change in practice [13].

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Stavroula A. Paschou conceived the idea of the editorial and wrote the initial draft.

Dimitrios G. Goulis revised the manuscript.

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Nikolaos Papanas conceived the idea of the editorial and revised the manuscript.

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