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# Diet and lifestyle for post-reproductive health: Focus on diabetes

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The prevalence of type 2 diabetes mellitus (T2DM) is 5 to 10% in western countries, while a large percentage of patients remains undiagnosed [1]. Menopause represents the end of reproductive life of women and is associated with metabolic changes which predispose to T2DM. One of the most prevalent phenotypical changes noted after menopause is weight gain. The decrease in estrogen concentrations leads to an increase in total body fat, specifically central abdominal fat accumulation. The abdominal obesity results in additional physical and psychological morbidity, initiating a vicious cycle. Excessive energy intake, sedentary lifestyle and stress are environmental factors that are often present during menopause and further contribute in the development of central obesity [2]. In turn, abdominal fat deposition leads to low grade inflammation and insulin resistance, through the action of cytokines and adipokines. Pancreatic β-cells have then to compensate insulin resistance in order to maintain normal glucose levels. Ultimately, only a subgroup of women with central obesity in menopause will demonstrate

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impaired glucose metabolism and T2DM. The genetic predisposition of  $\beta$ -cell dysfunction seems to constitute a crucial parameter [3].

Interestingly, women with climacteric symptoms present greater risk for development of diabetes [4]. Various animal and human studies have provided evidence that hormone replacement treatment (HRT) can ameliorate the tendency towards central obesity after menopause, with improvement of insulin sensitivity and reduction of the risk for T2DM. In large randomized controlled trials, T2DM incidence was decreased from 12% to 21% in women on HRT, with significant improvement of central adiposity, insulin resistance, lipids levels and inflammation markers [5]. However, HRT cannot be provided forever and there is not enough evidence to support administration of HRT for T2DM prevention [4,6]. Clearly, more research data are required in order to identify those women most likely to gain metabolic benefits from HRT.

Diabetes is broadly considered to be a cardiovascular disease equivalent, which would suggest that women with the disease should not take HRT. However, women with established T2DM show better glycemic control and demand lower doses of antidiabetic agents when on HRT. Unfortunately, clinical trials so far were not powered enough to assess differences in cardiovascular outcomes. It seems that HRT is beneficial in early menopause for women with T2DM, while in older women with mature atherosclerotic plaques this kind of therapy may

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destabilize them, resulting in acute thrombotic episodes. An individualized approach in treating menopausal symptoms should be considered with a low threshold to recommend non-hormonal therapies, particularly in women with concurrent cardiovascular disease. Some women with T2DM may be excellent candidates for HRT, following careful evaluation of their cardiovascular risk [2,6].

Excessive body weight is an important predictive marker of increased risk for T2DM, but also for other morbidities in later life, such as cardiovascular disease, sexual dysfunction, depression and deterioration of the general quality of life. Therefore, the most rational strategy for preventing T2DM is treating excess weight. We cannot modify genes, we are not able to stop the transition to menopause, we cannot provide HRT forever, but we can manage essential elements of lifestyle in post-menopausal women. Indeed, weight loss has been associated with longevity in patients with T2DM, even with remission of the disease, when very low calories programs were followed. Furthermore, two major trials, the Diabetes Prevention Program (DPP) and the Look AHEAD (Action for Health in Diabetes) study, have provided robust evidence for the beneficial effects of weight loss in patients with T2DM. Lifestyle intervention resulted in higher benefits regarding diabetes progression, HbA<sub>1c</sub> levels and cardiovascular risk factors [3].

Recommended diet and lifestyle changes for post-reproductive health with focus on T2DM should include modest weight loss, 5% to 7% of the initial body weight. This can be accomplished by lifestyle programs that provide 1200–1500 kcal per day or achieve an energy deficit of 500-750 kcal per day. Carbohydrates should derive from high-fiber and lower glycemic index foods, such as whole grains, vegetables, fruits, legumes and low-fat dairy products. Mediterranean diet, with high consumption of plant-based foods and olive oil, moderate consumption of fish and low consumption of red or processed meat has resulted not only in weight loss but also in cardiovascular benefits for patients with T2DM [1]. Bone health and sarcopenia is another important concern during the post-menopausal period. Therefore, modest and gradual weight loss should be advised. Consumption of nuts and seeds, appropriate intake of calcium and vitamin D, limited intake of alcohol and sodium represent additional lifestyle changes. Regarding exercise, intense walking at least 150 min per week seems ideal. Aerobic exercise of moderate intensity is indicated for patients with obesity and T2DM, while weight-bearing exercise is ideal for bone strength and quality. Intense walking combines both types of exercise, but also it offers psychological balance and preserves muscle mass. Finally, as smoking cessation is very important for both the reduction of endothelial dysfunction and osteoporosis risk, such counseling should be a routine parameter of the health care of all women in menopause [1,3].

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