EDITORIAL

An intervention to reduce vasomotor symptoms and induce weight loss at the menopause transition: can we really get two for the price of one?

Lee P. Shulman, MD

The onset of the menopausal transition invariably leads to a variety of lifestyle changes, with the onset of vasomotor symptoms and menstrual bleeding changes being two of the more common complaints of women in their 40s and 50s. However, a common concern of many women during this time in their lives is weight gain and increasing abdominal girth. All who care for women during menopause transition have heard this familiar story: despite eating only small amounts of vegetables and low-fat proteins and increasing their exercise activities, the past several months have not only witnessed an increase in weight of several pounds but also a change in how clothes fit, with an increasing sense of tightness in her clothing at her waist.

Although the onset of vasomotor symptoms and bleeding changes in menopausal transition commonly lead women to seek relief by visiting a clinician or self-medicating with nonprescriptive supplements or untested interventions, it is weight gain and change in body habitus that may be the most important clinical signs of the menopause transition. In the United States, nearly two-thirds of women aged 40 to 59 years and approximately 75% of women 60-years-old and older are overweight, with about half of these women being obese. The adverse health impact of being overweight or obese at any age cannot be overstated; for women entering menopausal transition, being overweight considerably increases the risk for metabolic syndrome, cardiovascular disease, some malignancies such as endometrial cancer and death.

The increased morbidity and mortality associated with being overweight or obese has been well known for years; however, the factors that promote weight gain and obesity in midlife women remain a complex and poorly understood interaction of physiological and lifestyle factors. Aging has long been associated with weight gain in both sexes; surprisingly, the onset of menopause does not appear to specifically impact weight gain when adjusted for age-related effects.

The impact of aging on increased body weight is primarily the result of physiological changes that lower the metabolic rate, reduce lean body mass, and for many women and men, reduced physical activity. Nonetheless, the onset of menopause does promote weight gain through other mechanisms, primarily related to the loss of endogenous estrogen and its associated onset of sleep disturbances, mood alterations, and other lifestyle changes. The loss of endogenous estrogen is also strongly related to central fat accumulation, which can be perceived as weight gain even by women who have not gained weight and is in itself associated with increased physical and psychological morbidity.

Menopausal hormone therapies (MHTs) have been shown to be effective in reducing menopause-related vasomotor symptoms, but studies have generally not found a weight-reducing effect for women using MHTs. However, the use of MHTs has been associated with improvements in lean body mass, insulin resistance, and lipid levels as well as a decrease in abdominal fat. Interestingly, an over-the-counter dietary supplement containing a proprietary succinate formulation was studied in two trials that were relatively small in size and short in length (90 d) but were randomized, placebo-controlled, and double blinded and demonstrated a reduction in menopause-related symptoms and modest weight loss among women who were randomized to the active drug cohort. As such, a pharmacological intervention that would reduce vasomotor symptoms and be shown to potentially lead to weight loss would be an important addition to the menopausal therapy armamentarium for women suffering from the symptoms of menopausal transition.

In this issue of Menopause, Kapoor et al publish their results from a pilot study of lorcaserin, a selective serotonin 2C (5-HT2C) receptor agonist that has been previously approved by the FDA for weight loss but recently recalled due to an increase in cancer risk compared to placebo. Anecdotal reports of reductions in vasomotor symptoms among users had been observed and was the impetus for performing this pilot study. The authors recruited 20 overweight “midlife” women who were found to have “bother-some vasomotor symptoms (VMS), defined as 28 or more hot flashes per week that were present for more than 30 days, and were of sufficient severity to prompt them to seek therapeutic intervention.” All 20 participants used lorcaserin (Belviq Eisai, Tokyo, Japan) at the recommended dose of 10 mg
orally twice a day for 12 weeks. The authors reported that 90% of the participants completed the 12-week study; significant reductions in weight and severe/very severe hot flushes were observed. Two women withdrew from the study because of headaches and one participant reported seizure-like activity after conclusion of medication usage.

This study provides an excellent foundation for future studies of drugs similar to lorcaserin without risks for cancer as a treatment for vasomotor symptoms and weight gain associated with menopausal transition. Clearly, more robust studies will be needed to properly evaluate the effectiveness and safety of this drug regimen. It behooves all of us to recognize that there is likely no one “‘magic pill’” that will miraculously help menopausal women lose weight and the symptoms of menopause over the course of their lives. Although weight gain observed among many menopausal women is associated with some menopause-related symptoms, weight gain is also strongly associated with an aging process that is likely not amenable to a single drug regimen. Our experience tells us that proper weight management is a combination of lifestyle modification, increased physical exercise and the use of specific medications in some individuals who may benefit from the amelioration of certain unique physiological factors that are not necessarily found in many or most other people. We want to believe that simply taking a pill will get us to our health and lifestyle goals, but for the vast majority of us, it’s just not so.

Juan Ponce de Leon is said to have sought to find the “‘Fountain of Youth.’” Instead, he landed in Puerto Rico and St. Augustine, Florida: wonderful and important locales, but not the Fountain of Youth. It is good to have lofty goals, but in the end those goals must not cloud our judgment or our knowledge of science and medicine. Lorcaserin has been shown to reduce hot flushes and body weight in a 12-week, open label study of 20 overweight symptomatic menopausal women. The authors are to be congratulated for taking a first step in evaluating a new and potentially important field of drug therapy, but let’s not yet celebrate the end of diet and exercise in our seemingly never-ending quest for a quick and easy weight loss and symptom-reducing menopausal regimen. At least not until we have more robust studies assessing the safety and effectiveness of drugs like lorcaserin or other future drug candidates.

REFERENCES