CME CREDIT

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BRIEF ANSWERS TO SPECIFIC CLINICAL QUESTIONS

Q: What are the key issues women face when ending hormone replacement therapy?

WULF H. UTIAN, MD, BCH, PhD*
Department of Obstetrics and Gynecology, The Cleveland Clinic; Professor Emeritus, Case Western Reserve University; Executive Director, The North American Menopause Society

A: The Women's Health Initiative[1] has thrown physicians and patients into a quandary about hormone replacement therapy (HRT).

On one hand, this landmark study laid to rest the question of whether continuous combined estrogen-progestin replacement therapy prevents cardiovascular disease (it doesn't) and delineated the potential risks. On the other hand, it provided no answers to some key issues women face if they choose to stop HRT.

The following comments mostly apply to continuous combined estrogen-progestin therapy, since it was this arm of the Women's Health Initiative that was terminated early due to increased rates of coronary artery disease, breast cancer, stroke, and pulmonary embolism. The estrogen-only arm, in women without a uterus, is continuing without evidence of excess risk at this time.

WHY IS THE PATIENT ON HRT?

A logical approach is to review why the patient is on HRT and to consider alternatives.

If she has no indication for HRT

Surprisingly many women have been on estrogen-progestin therapy for long periods of time, but are uncertain as to why they are on it. In this situation, it is logical to stop the HRT.

If she has vasomotor symptoms

Most women on HRT started because of vasomotor symptoms, and more than 75% stop within 24 months.[2] Those who stop and then start again invariably do so because of a recurrence of severe symptoms.

These patients who wish to stop HRT can be advised to try alternatives such as clonidine, selective serotonin reuptake inhibitors, or beta-blockers, but none of these therapies provide the level of effect of HRT, and most carry their own set of potential side effects.

Many women try over-the-counter herbal products. These are essentially no more effective than placebo, which can actually be of short-term benefit in up to 40% of women.

In practice, women with severe recurrent symptoms are the most difficult to advise. The strategy should be to carefully explain the known level of risk and to give the patient the option of restarting on a low-dose regimen under continuous scrutiny.

If she is on HRT to prevent osteoporosis

If the patient is on HRT to prevent osteoporosis, alternatives are available, including the selective estrogen receptor modulator raloxifene and the bisphosphonates alendronate and risedronate.

Remember that women who stop HRT are likely to experience the rapid bone loss that is typical of postmenopause.[3] It is therefore wise to obtain dual-energy x-ray absorptiometry (DEXA) scans of the hip and spine when stopping HRT and to repeat them at least 1 year later unless alternative bone-sparing therapy is started immediately.

The real dilemma is how to advise a woman who entered menopause early (ie, at age 40 to 50 years) or prematurely (ie, younger than age 40). In this situation I am less confident about ultra-long-term treatment with bisphosphonates and would prefer raloxifene

Review why the patient is on HRT, and consider alternatives

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or HRT, at least until the usual expected age of menopause around age 50.

If she is on HRT for quality-of-life issues

The Women's Health Initiative did not address a variety of conditions that estrogen-progestin therapy may or may not improve, such as vaginal atrophy and problems with the skin, teeth, and gums, cognitive function, mood, sleep, sexuality, and quality of life (appropriately measured by a validated instrument such as the Utian Quality of Life Scale).[4]

Many women experience subjective negative feelings when they stop HRT and state they "feel better" on hormones. These responses are difficult to quantify, but women often weigh them heavily in favor of continuing HRT when they consider risk and benefit issues.

Unfortunately, there is no one alternative therapy to address each of these issues. Vaginal atrophy is easily corrected by use of low-dose vaginal estrogen cream or vaginal tablets and rings. This certainly benefits women suffering discomfort with intercourse, but will not enhance libido. While androgens are sometimes considered, there are few data on long-term safety or efficacy. Cognitive function and mood are best approached through counselling or selective use of psychopharmacotherapeutic agents. Overall quality of life is best enhanced by counselling, exercise, healthy diet, and lifestyle changes.

Order a DEXA scan when a patient stops HRT, and repeat 1 year later

HRT to prevent cardiovascular disease

Postmenopausal women should clearly stop taking estrogen-progestin therapy if they have no symptoms and are taking it only for cardiovascular protection. It is essential, however, to define their cardiovascular risk factors and treat these accordingly, for example with antihypertensive or lipid-lowering drugs.

IMMEDIATE BENEFIT VS FUTURE RISK

Women thus face the dilemma of balancing the mostly immediate benefits of HRT against its future risks.

Breast cancer risk, the principal concern, increases with duration of HRT.[5] In contrast, the risks of cardiovascular disease, stroke, and venous thromboembolism appear to reach a plateau in the first 1 to 2 years of HRT but go no higher with long-term use.[1,6] Indeed, alternate routes of administration or lower doses of HRT may not demonstrate any early increase in risk of cardic events or stroke.[7] Because coronary heart disease, stroke, venous thromboembolism, and osteoporotic fractures are less common in younger women, the absolute risks and benefits will be lower in the short term in younger women.[8]

The challenge to the health care provider is to identify women at risk of complications before they start HRT, so that these women can be advised of appropriate alternatives to HRT.

TAPERING VS COLD TURKEY

Women who stop HRT need practical advice on how to stop taking the medication, but there is no guidance from the existing medical literature. One can either stop abruptly ("cold turkey") or taper off therapy by either skipping progressively more days between doses or lowering doses every 4 to 6 weeks. A past history of severe symptoms may favor tapering.

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ADDRESS: Wulf H. Utian, MD, Executive Director, The North American Menopause Society, 5900 Landerbrook Drive, Cleveland, OH 44124; e-mail utian@menopause.org.