Menopausal hormone therapy

(AUGUST 2016)

TO THE EDITOR: I much enjoyed the important article by Drs. Lipold, Batur, and Kagan on whether there is a time limit for systemic menopausal hormone therapy.[1] The simple answer is no. The authors did a good job of reviewing the factors to consider in terms of contraindications and precautions when prescribing menopausal hormone therapy.

An important part of the discussion regarding stopping hormone therapy is the recent evidence from Finland that has shown increased risks of myocardial infarction and stroke, especially in women under age 60, when taken off hormone therapy.[2] This fact is quite ironic, as many clinicians are trying to rush to get women off hormone therapy in order to protect the heart, when the evidence does not suggest this. Just as with other hormone-deficiency conditions, the status needs to be periodically reviewed, and doses may need to be adjusted. However, after age 60 or 65, women do not automatically start producing the sex hormone that they have been deficient in. While menopause is not a definite endocrinopathy, it is a potential endocrinopathy; and for some women, such as young women who are oophorectomized, it is an absolute endocrinopathy.

The International Menopause Society has published updated guidelines emphasizing that new data and reanalysis of older data show that for most women the benefits of menopausal hormone therapy are much greater than the risks, particularly when started within a few years of menopause.[3]

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IN REPLY: We would like to thank Dr. Thacker for her interest in our article on the clinical considerations regarding optimal duration of hormone therapy.[1] We agree that the simple answer to whether there is there a time limit for systemic menopausal hormone therapy is no, emphasizing an individualized approach to each patient. After appropriate counseling and shared decision-making, some women may elect a short duration of therapy while others prefer longer-term use.

As Dr. Thacker mentioned, Mikkola et al[2] performed an observational study of more than 300,000 Finnish women who discontinued hormone therapy. Data on the number of deaths in this group were gathered from a national database and compared with the expected number of deaths in the background population; 30% of the listed causes of death were confirmed by autopsy. In women who had started hormone therapy before age 60, the risk of cardiac death was elevated within the first year after stopping it (standardized mortality ratio [SMR] 1.74; 95% confidence interval [CI] 1.37–2.19), as was the risk of stroke (SMR 2.59, 95% CI 2.08–3.19). This was not true in women who started hormone therapy at age 60 and older. These findings are consistent with our contemporary understanding that for many women younger than age 60 the benefits of hormone therapy outweigh the risks.

The study had several important limitations:

- A healthy-woman bias may have contributed to the reduction in cardiovascular risk.
- No dates for the myocardial infarctions or strokes were available, and the dates hormone therapy was discontined potentially had a 3-month error.
- No data were available on important confounding factors such as smoking, body

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mass index, blood pressure, lipid levels, and family history.

- Hormone therapy users were compared with an age-standardized background population, which also included hormone therapy users.
- Long-term follow-up data were also perplexing: although more women than expected died of stroke or coronary heart disease within the first year of stopping hormone therapy, after 1 year, significantly fewer women died of these conditions than expected, regardless of how long they had been on hormone therapy before stopping.

These observations highlight the need for long-term, randomized, prospective controlled studies that adequately assess all long-term outcomes (cardiovascular events, mortality, cancer, fracture) in women who initiate hormone therapy before age 60 and within 10 years of menopause, including long-term follow-up after discontinuation. Though future randomized controlled trials will be beneficial to help guide women to a more balanced understanding of long-term hormone therapy and the risks of discontinuation, the current evidence supports continuing hormone therapy in women who derive a net benefit.

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