

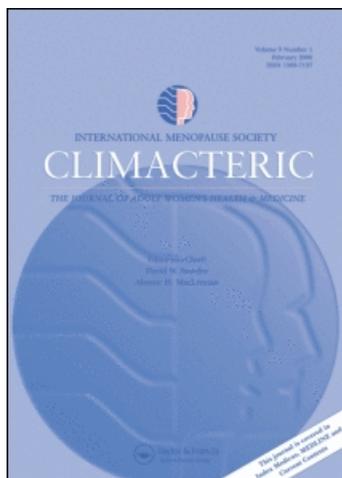
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## The HERS trial

M. Neves-e-Castro <sup>a</sup>

<sup>a</sup> Av. António Augusto, Lisbon, Portugal

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## Letter to the Editor

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### The HERS trial

The conclusions of this study were not at all what everybody expected on the basis of many observational studies that found a protective effect of estrogens on coronary heart disease (CHD). The HERS Research Group concluded<sup>1,2</sup> that the treatment (0.625 mg of conjugated estrogens plus 2.5 mg of medroxyprogesterone acetate in one tablet daily) 'did increase the rate of thromboembolic events and gallbladder disease' and found 'no overall cardiovascular benefit and a pattern of early increase in risk of CHD'. Thus they 'do not recommend starting this treatment for the purpose of secondary prevention of CHD.'

As a gynecologist-endocrinologist with a large practice, mainly attended by menopausal women, with long follow-ups and a very low drop-out rate, I am disappointed with certain aspects of the HERS trial and the lack of important information.

First, when indicated, I prescribe HRT to women younger than 80 years, the age of the patients in the study. I also treat many women with a mean age of 66 years, again like those indicated in this study. However, I have very seldom used more than half of the doses of estrogen given in this study or the progestogen that was added. I monitor the effects and side-effects of the medication and I adjust it appropriately. My results are very satisfactory, be they in terms of the cardiovascular system, bone, lipids or the quality of life.

Therefore, the protocol which was adopted in the HERS trial does not reflect what I consider, from my experience, the best way to administer HRT. These older women require lower doses, which are nevertheless effective.

Second, I therefore presume that the women in the HERS trial were *overmedicated!* The 10% difference in compliance, at the end of the first year, suggests that the estrogen + progestin group had a higher drop-out rate due to signs and symptoms of *overdose*, namely mastalgia, spottings,

uterine bleedings, etc. This was confirmed at my request by some of those involved in the study, during a private meeting that I attended<sup>3</sup>.

Third, the final report<sup>1</sup> does not indicate whether the estrogen + progestin groups had gained more weight than the placebo group; whether there were differences in blood pressure between the groups; whether the women who suffered from the events (fatal or not) were those with clinical manifestations of excessive treatment; and whether the results of the autopsies in the estrogen + progestin and placebo groups suggested any differences.

Last, it would be of great interest to recalculate the results which were observed in the estrogen + progestin group divided into several subgroups of women, namely those with clinical signs of overdose (mastalgia, spottings, uterine bleedings), those with weight gain and those with increased blood pressure.

I would not be surprised if the conclusions had to be reformulated.

Av. António Augusto  
Aguiar 24-2 DT  
Lisbon 1050-016  
Portugal

M. NEVES-E-CASTRO

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