

Hormone Therapy Controversy

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I am writing this article in an effort to bring some balance to the confusing and alarming headlines stemming from last summer's results from one arm of the Women's Health Initiative (WHI) study. [1] I have witnessed a troubling trend as a result of the media reports. I am seeing more women coming in whose physicians and healthcare providers have taken them off their hormone therapy because of the study. My intention in writing this piece is to put in perspective the importance of the WHI results released last summer, which although individually important because of the size and rigor of the study design, is ultimately just one more study in the larger continuum of historical and ongoing studies and their combined results regarding hormone therapy for women.

To quote from Patricia Kelly, PhD, "the results of the WHI studies have been presented as conclusive evidence that all hormone replacement therapy increases breast cancer risk and does not reduce cardiovascular disease risk. This interpretation is out of proportion to the findings and overlooks evidence suggesting that the very small differences in risk between the study and control groups in these studies may not be due to *Prempro*[®] use." [2]

Dr. Kelly is a medical geneticist affiliated with Saint Francis Memorial Hospital in San Francisco. She has provided Cancer Risk Assessment for twenty-five years and is particularly interested in developing effective ways

to integrate cancer risk information into general medical practice.

As it pertains to breast cancer she wrote, "very small differences in risk were found between the study and control groups." The results of the WHI study showed, "there was an annual increase of eight breast cancers in 10,000 women - an increase of eight hundredths of one percent. This exceedingly small difference was not statistically significant. The breast cancer risk in the WHI study was repeatedly reported as 1.29, or a 29% increase. Many did not realize that this 29 percent increase was, in absolute terms, only eight hundredths of one percent. Such misunderstandings frequently occur when risks are reported as percent differences instead of in actual, absolute terms." [2] Did hormone therapy cause the breast cancer? WHI did not answer this. We know it takes at least 8 years for breast cancer to become clinically detectable. The study ended after approximately 5 years of hormone use. In *Prempro*[®] users, 84 percent of the breast cancers were found in the first five years. [1] This means that all or nearly all breast cancers found in *Prempro*[®] users were present in undetectable state before the study began.

In terms of cardiovascular disease Dr. Kelly continues on to write that, "Differences in cardiovascular disease rates were quite small in the WHI study, *Prempro*[®] users had seven additional cases of heart disease and eight of stroke annually in 10,000 women. With

the exception of thrombosis, none of these differences was statistically significant when results were adjusted." [2] The issue of the reduction of coronary heart disease with use of hormone therapy was raised initially in the 1970's. There has been around 300 published reports including 130 papers on open trials and 165 randomized trials. Until recent data from the WHI, the consensus was that the risk of coronary heart disease (CHD) was 35-50% lower in women using estrogen replacement. There was particular emphasis on the favorable effect on the lipid profile (increase in HDL-C, decrease in LDL-C, and Total Cholesterol Concentration) as well as the beneficial effect on vascular endothelial function. [3]. For instance, the highly respected Nurse Health Study showed a 50% reduction in risk. The differing rate of cardiovascular disease (CV) probably stems from the nurses starting their hormone therapy at the time of menopause. The WHI represented more elderly women who were asymptomatic but not disease free and started hormone therapy well after menopause. Can we really say the hormone therapy provides no CV protection? The WHI did not answer this question as it was not a primary prevention trial.

On the positive side the risk reduction for colon cancer demonstrated by the WHI with combined hormone therapy was approximately 37% (it is important to keep in mind women are 3

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times more likely to die from colon cancer than breast cancer). The study also showed that hormone therapy significantly reduced the risk of fracture, especially hip and vertebral fracture, which were reduced by one-third. [1]

Women deserve to see the "whole picture" and then base their decision on informed consent, balancing the risk and benefits as it relates to them specifically. Nothing in medicine is ever "black and white." You don't throw out over twenty years of research because of one study, no matter how impressive its clinical design, because that study says something different. We in woman's health have spent the last year trying to make sense of the study and why its results were unexpected. Unfortunately, in the meantime, women are confused, afraid, and are being denied known treatment for their menopausal symptoms.

Remember there are many other documented benefits to hormone

therapy:

- prevention of glaucoma
- treatment of low grade depression
- treatment for sleep disturbance
- prevention of urogenital atrophy
- prevention and treatment of sexual dysfunction
- treatment for memory disorder
- maintenance of skin turgor and elasticity
- possible prevention of Alzheimer's Disease [4]
- the continuing possibility of primary prevention of coronary heart disease.

Menopause and hormone therapy is a complex puzzle, and I encourage you to look beyond the headlines. There are risks and benefits associated with all treatments. Let's work together, not against one another, in this area to improve the quality of care for our women patients. We each have a unique perspective and training that helps balance our patient's needs. It is our obligation as clinicians to keep up with the literature in our respective areas of expertise and to recognize our limitations.

References

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