The Effect The Women's Health Initiative Study (WHI) in July 2002 had on Management of Menopause: A Literature Review

Author - Lauren Morris, lauren.morris@sa.gov.au Affiliations - The Lyell McEwin Hospital, Adelaide

Introduction: Symptoms of menopause are a common reason women seek Hormone Replacement Therapy (HRT). The Women's Health Initiative (WHI) was a US multi outcome study, which included an arm examining the suggested reduction in the risk of cardiovascular disease in post-menopausal women using combined HRT. This study had over 16,000 participants and was designed to last 8.5 years, however it was ceased after 5.2 years due to an unacceptable increase in adverse outcomes, including breast cancer. The aim of this review is to determine the effect the WHI findings had on the use of combined HRT.

Methods: Literature review of available studies and publications.



Results: The initial and ongoing response to the WHI study was wide and variable. Peer reviewed journal articles were published both in support and in dispute of the findings. Many publications examined the existing data from the WHI as well as new data on the subject. The conclusions of many of these reviews did not support the findings of the WHI.

Discussion: The findings of the WHI had a broad impact on the use of HRT in the management of menopause and sparked significant debate in the safety of HRT. Ongoing research is required in the area to conclude on the long term safety of HRT, however it is generally accepted that combined HRT for 5 years or less in the immediate post-menopausal period is not associated with a significant increase in breast cancer risk. This conclusion is supported by current RANZCOG guidelines. The findings of the WHI were widely misinterpreted and incorrectly extrapolated, resulting in major changes to the way HRT was used in the management of menopause.

References:

- 1. Study TW. Design of the Women's Health Initiative clinical trial and observational study. Controlled clinical trials. 1998 Feb 1;19(1):61-109.
- 2. Lobo RA. Where are we 10 years after the Women's Health Initiative?. The Journal of Clinical Endocrinology & Metabolism. 2013 May 1;98(5):1771-80.
- 3. Clark JH. A critique of Women's Health initiative studies (2002-2006). Nuclear receptor signaling. 2006;4.
- 4. Chlebowski RT, Hendrix SL, Langer RD, Stefanick ML, Gass M, Lane D, Rodabough RJ, Gilligan MA, Cyr MG, Thomson CA, Khandekar J. Influence of estrogen plus progestin on breast cancer and mammography in healthy postmenopausal women: the Women's Health Initiative Randomized Trial. Jama. 2003 Jun 25;289(24):3243-53.
- 5. Lacey Jr JV. The WHI ten year's later: An epidemiologist's view. The Journal of steroid biochemistry and molecular biology. 2014 Jul 1;142:12-5.
- 6. Burger H. Hormone replacement therapy in the post-Women's Health Initiative era. Report as meeting held in Funchal, Madeira, February 24-25, 2003. Climacteric: the journal of the International Menopause Society. 2003 May;6:11-36.
- 7. Day A. Lessons from the Women's Health Initiative: primary prevention and gender health. Cmaj. 2002 Aug 20;167(4):361-2.
- 8. Harman SM. Estrogen replacement in menopausal women: recent and current prospective studies, the WHI and the KEEPS. Gender medicine. 2006 Dec 1;3(4):254-69.
- 9. Australian Menopause Society, Women's Health Initiative Update, 2013, [cited 23 April 2019], available from: https://www.menopause.org.au/hp/news/857-womens-health-initiative-update-2013