



BENEFITS AND RISKS OF COMBINED (ESTROGEN AND PROGESTIN) HORMONE REPLACEMENT THERAPY

The Issue

For many years, women have been prescribed combined estrogen and progestin Hormone Replacement Therapy (HRT) to relieve some of the symptoms of menopause. However, recent scientific studies have identified significant risks associated with this therapy.

Background

HRT products have been approved by Health Canada to treat menopausal symptoms such as hot flashes, night sweats, vaginal dryness and in some cases, to prevent osteoporosis. While there are other forms of hormone replacement available, such as the patch, gel and vaginal ring, HRT is most commonly taken in pill form, of which there are two main types:

- combined (estrogen and progestin)
- estrogen without progestin

Progestin is added for the prevention of uterine cancer in women who have not had a hysterectomy (surgical removal of the uterus).

Some earlier studies suggested that the use of HRT products might help to prevent heart disease in post-menopausal women. But the lower incidence of heart disease among these women is now believed to be due to other factors such as diet and lifestyle. The labelling materials approved by Health Canada for HRT products clearly state that they have not been approved for the prevention of heart attack, stroke or any other cardiovascular disorder.

The Health Risks and Benefits of HRT

In 1991, the U.S. National Institutes of Health (NIH) launched the Women's Health Initiative (WHI), a set of studies involving healthy post-menopausal women that was carried out in 40 U.S. centres. The WHI included a clinical trial to evaluate the risks and benefits of the two types of HRT (administered in pill form) and to see how they affected the incidence of heart disease, breast cancer, colorectal cancer and fractures in post-menopausal women. The trial was divided into two arms:

- One arm involved more than 16,000 post-menopausal women aged 50 to 79 who had not had a hysterectomy. They took pills daily that were either a combination of estrogen (equine conjugated estrogens 0.625 milligrams) and progestin (medroxyprogesterone acetate 2.5 milligrams), or a placebo (pills with only inactive ingredients).
- The second arm involved more than 10,000 women who had had a hysterectomy and who took estrogen pills alone or a placebo.

In July 2002, after an average 5.2 years of regular follow-up, the NIH prematurely ended the combined (estrogen and progestin) HRT arm of the WHI trial. An independent monitoring board, which regularly reviewed the findings, concluded that there were more risks than benefits among the group using combined HRT, compared with the placebo group. The study found that changes in the incidence of disease per 10,000 women on combined HRT in one year were:

- Seven more cases of coronary heart disease (37 on combined HRT versus 30 on placebo)
- Eight more cases of strokes (29 vs 21)



- Eighteen more cases (34 vs 16) and a twofold greater rate of total blood clots in the lungs and legs
- Eight more cases of invasive breast cancer (38 vs 30)
- Six fewer cases of colorectal cancer (10 vs 16)
- Five fewer cases of hip fractures (10 vs 15)

While these numbers appear to be low, they are highly significant. Given that millions of women are taking combined HRT, the number affected over many years is an important public health issue.

Since July, 2002, further results from the Women's Health Initiative trial have been published. Among the findings:

- In a subgroup of more than 4500 women aged 65 or older, an additional 23 cases of dementia in 10,000 women per year were reported among women on combined HRT, as compared to placebo (45 vs 22). As well, combined HRT did not prevent mild cognitive impairment among women who used it and there was a small increased risk of cognitive decline in the combined HRT group.
- Compared to non-use of HRT, the use of combined HRT increases breast density and was shown to compromise the interpretation of mammography results.

In light of these results, combined estrogen and progestin are not recommended for long-term use in post-menopausal women, except in limited circumstances where other therapeutic choices are found inadequate. The risks of breast cancer, blood clots, stroke, coronary heart disease and dementia (in women aged 65 and over) are considered to outweigh the benefits of fracture reduction and the reduced risk of colorectal cancer, when long term use of HRT is considered.

Since there is no clear indication as to what happens when progestin is not part of the HRT, the estrogen-only arm of the WHI trial is continuing. Current knowledge suggests an association between prolonged use of estrogen-only therapy and a slight increase in breast cancer. An answer is expected by 2005.

Please note that other dosage levels of combined HRT and other forms, such as the patch, gel or vaginal ring, were not examined in this study.

Minimizing Your Risk

The decision to use HRT should be based on your particular needs and health, and made after a careful medical evaluation. If you are taking or considering taking HRT, you should:

- Discuss with your doctor the benefits and risks of the various forms and dosage levels of HRT in light of your medical history.
- Talk to your doctor about how to manage menopausal symptoms and any post-menopausal conditions. For example, there are effective alternative therapies for osteoporosis.
- Eat a healthy diet, exercise regularly, drink alcohol only moderately and do not smoke. These are important steps to prevent osteoporosis and coronary heart disease.
- You should not use combined HRT for the prevention or treatment of coronary heart disease or stroke.
- Combined HRT is effective for the control of hot flashes, night sweats and vaginal dryness. However, even short-term use is associated with an increased risk of blood clots, stroke and coronary heart disease. HRT should only be used if your symptoms are severe and if you have been fully informed of the risks. HRT

requires regular medical evaluation.

Health Canada's Role on HRT

Health Canada is continuing to monitor the benefits and risks associated with HRT, through pre-market reviews and post-market surveillance. Doctors and consumers will be updated on new findings as they are reported. Health Canada is also updating a comprehensive document on menopause. This publication will be posted on the Health Canada Web site as soon as it is available.

Need More Info?

For more information on menopause and HRT, contact:

Canadian Women's Health Network
<http://www.cwhn.ca>

North American Menopause Society
<http://www.menopause.org>

Society of Obstetricians and Gynecologists of Canada
www.sogc.medical.org

For more information on the NIH study, contact:

NIH Women's Health Initiative
<http://www.nih.gov/PHTindex.htm>

For more information on Breast Cancer see the It's Your Health article at:
http://www.hc-sc.gc.ca/english/iyh/diseases/breast_cancer.html

Additional It's Your Health articles can be found at:
www.healthcanada.ca/iyh
You can also call (613) 957-2991

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