Hormone Replacement

What's the Controversy?

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There is increasing awareness of the risks and benefits of hormone replacement therapy (HRT) in women.

There have been two recent studies, namely the Heart, Estrogen/progestin Replacement therapy Study (HERS) and the Women's Health Initiative (WHI), which have forced us to re-evaluate HRT.[1,2]

WHI

The WHI is a momentous study in women's care and has the most accumulated observational evidence of major health benefits and risks commonly associated with HRT. In this study, there is a distinction made between estrogen replacement therapy (ERT) and hormone replacement therapy (HRT).

The WHI involved 40 U.S. clinical centres and had a planned duration of 8.5 years. Women aged 50 to 79 were enrolled in the study; the average age of entry was 63.2. There were two arms of the study: conjugated equine estrogens/progestin combination and estrogens only. The first arm of the study was discontinued because of increased risk of breast cancer.[3]

The estrogen-only arm was discontinued in March 2004 because of increased risk of strokes and venous thromboembolic disorders.

Beneficial aspects of the WHI trial include fewer colorectal cancers and hip fractures. Overall, cancer rate is not affected with the use of HRT.

Estrogen administration also reduces the risk of developing Alzheimer's disease, but does not affect the progression of the disease.

WHI is not without criticism, however. Two-thirds of the

Quick Point

WHI: Absolute excess risk per 10,00 persons on HRT:

7 more coronary heart disease events

8 more strokes

8 more pulmonary embolisms

8 more invasive breast cancer cases

Michelle's case

Michelle, 54, is a G2P2 woman. She presents complaining of hot flushes, insomnia and moodiness since she discontinued her estrogen replacement therapy (ERT).

She had been taking oral estrogen, 0.625 mg daily, for eight months following her total abdominal hysterectomy and bilateral salpingectomy for ovarian cancer. The cancer was stage 1 and she is currently disease-free.

She does not drink alcohol or smoke cigarettes. She is on calcium supplementation, 1,500 mg daily. She works out at a local health centre twice a week. Her family and social review are normal.

Physical exam is unremarkable, apart from dryness of her vagina. She had a recent mammogram, which was normal.

She wants to go back on ERT, but at the same time, wants to avoid the risk of breast cancer.

What should Michelle do?

Michelle decides to continue with ERT. Ovarian cancer is not a hormone-related cancer and, moreover, she is free of the disease. Her quality of life is much more important.

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Table 1

Post-menopausal alternatives for...

Cardiovascular risk reduction

- Lifestyle interventions (weight reduction, exercise, diet and smoking cessation)
- Statins
- Antihypertensive medications
- Low-dose acetylsalicylic acid

Osteoporosis risk reduction

- Lifestyle interventions
- Calcium, 1,000-1,500 mg/day; vitamin D, 600-800 IU/day
- Bisphosphonates (alendronate, etidronate, risedronate)
- Raloxifene
- Calcitonin

Vasomotor symptoms

- Lifestyle (exercise and stress reduction programs)
- Short-term estrogen therapy
- Selective serotonin reuptake inhibitors or venlafaxine
- Clonidine, 0.05-0.1 mg orally or transdermally twice daily
- Ergotamine
- Bromocryptine
- Veralipride, 100 mg daily
- Naloxone
- Tibolone, 2.5 mg daily
- Methyldopa, 50-1,000 mg/day
- Phyoestrogens
- Vitamin E, 800 IU daily
- Back cohosh, herbal mixtures, acupuncture (limited efficacy)

Genitourinary symptoms

- Non-hormonal vaginal moisturizers
- Vaginal hormonal options

women in the study were reported to fall into a moderate to high-risk category for stroke, with about 50% being current or past smokers and 30% having hypertension.

Further, analysis of the women in the WHI trial revealed over one-third of the women were at high-risk for diseases associated with obesity.

So, what's the controversy?

- The effects of estrogen and progestin on younger, healthier women are not yet known.
- The effect of lower dosage treatment regimen is also unknown.
- The effects of prometrium and other progestogens in combination with estrogen have not been explored.
- Other unknown territory is the transdermal route application; routes of administration may produce different results.

What is the GP's role?

Informed choice regarding assessment for breast cancer should be undertaken by every medical practitioner. Other benefits of HRT should also be highlighted. Quality of life is more important than abrupt stoppage of treatment.

Dosage should be decreased slowly. Another option is to use HRT on alternate days for several days, otherwise withdrawal bleeding may occur.

Menopause brings many challenges to patients and physicians. It is now clear HRT is not the only solution to this problem and other options should be considered (Table 1).

Informed choice should be the goal in counselling women about HRT.

HRT should not be prescribed for primary prevention or secondary prevention of heart disease. Alternatives do exist and should be tried in women who feel uncomfortable with HRT. Dx

References

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2. Writing group for the Women's Health Initiative investigators: Risks and benefits plus progestin in healthy postmenopausal women: Principal results from the Women's Health Initiative randomized controlled trial. JAMA 2002; 288(3):321-33.
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