

MEDIA BACKGROUND

Menopause and Osteoporosis Update 2009

Purpose of the Update

The SOGC last updated its menopause-related clinical guidelines as part of its **Canadian Consensus Conference on Menopause** in 2006. New research in the area of menopause and osteoporosis, as well as new insights into past studies, prompted this 2009 update. The purpose of the most recent Update was to conduct a comprehensive review of the new scientific literature to obtain clarification on:

1. the use of hormone therapy for postmenopausal symptomatic women
2. the cardiovascular risks associated with hormone therapy
3. the breast cancer risks associated with hormone therapy
4. hormone therapy and osteoporosis fracture risk evaluation
5. whether or not age and symptoms are of importance when considering hormone therapy

Canadian Demographics

- Canadian demographics reveal that in the next decade, health-care professionals will see the largest population of newly menopausal women ever
- In Canada, there are now 2.5 million women between the ages of 45 and 54
- This generation of “baby-boomers” remains busier than ever, with family and business concerns. They want to remain active while minimizing distressing symptoms and medical consequences of menopause

The 2002 Women’s Health Initiative (WHI) Randomized Controlled Trial

Rationale

- A randomized controlled trial (RCT) to address the long-term benefits and risks of hormone therapy
- The ideal study would have recruited newly menopausal women who would agree to be randomly assigned to hormone therapy or placebo, and followed for ten to twenty years
- Difficult to find subjects willing to commit for the duration of the study, too long for an answer, too costly

Methodology

- The investigators recruited women in their 50s, 60s, and 70s
- It was the largest, most expensive study ever conducted by the National Institutes of Health in the USA
- Randomized controlled trials in two groups (16,000 women with a uterus and 10,000 women after hysterectomy) assessed effects of hormone therapy on cardio-vascular disease and breast cancer

Results

- The first reports stated that hormone therapy increased heart attack and stroke
- Subsequent reports emphasized increased risks of breast cancer and dementia
- The study was unable to assess the benefits of HT for vasomotor symptoms because most of the older population were not having hot flashes to start with
- The study confirmed the effectiveness of hormone therapy for the prevention of osteoporotic fractures

- A critical examination of the results did raise the question of whether or not the age of participants influenced the results. According to Hulley, age did matter. With regard to CHD (heart attack) risk and risk of blood clots:
 “Women in their 50s have half the (baseline) risk of women in their 60s and one quarter the risk of women in their 70’s.” (Hulley SB, Grady D. Editorial. JAMA 2004; 291 (14): 1769-1771)

Consequences of the Initial WHI Reports

- Both doctors and patients became fearful of hormone therapy
- Many doctors advised discontinuation of hormone therapy
- 50% of users in North America stopped hormone therapy
- The reluctance to prescribe hormone therapy caused many women to turn to complementary therapies
- A multi-billion dollar market in alternative and complementary products for the relief of menopausal vasomotor symptoms was fueled
- As many as a 25% of those who stopped hormone therapy returned to their doctors for “permission” to resume treatment
- Advice to “put up with the symptoms of menopause” ignored the fact that symptoms can be extremely disruptive, that they affect 65% of menopausal women and that, in most women, symptoms last for five to seven years, and in 15% of cases, for even longer
- Women felt they had no options and often suffered in silence

The Impact of Lifestyle Choices during Menopause

Lifestyle choices and modifications are often underestimated in terms of their capability to minimize the impact of menopause and aging

- **Vasomotor symptoms** (e.g. hot flashes, sleep disturbances) – Avoid triggers (e.g. alcohol and hot drinks); minimize heat retention by dressing in layers; exercise may help women with mild symptoms
- **Osteoporosis** – Family history is important but low body weight, smoking, lack of exercise, low intake of calcium and vitamin D, early loss of ovarian function, and certain medications all accentuate risk
- **Cardio-vascular disease** – Research has shown that 94% of cardio-vascular disease risk in women is attributable to modifiable risk factors such as weight, smoking, lipids, blood pressure, exercise, etc. (Yusuf S et al; INTERHEART Study Investigators. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study Lancet 2004; 364:937-52)
- **Cancer** – The minority of cancers are genetically linked. In the remaining population, cancer is a disease of aging and so lifestyle choices can profoundly impact cancer risk, e.g. Breast cancer (10% due to BRAC gene mutation), other factors: early menarche, late menopause, late first pregnancy (after age 30), reduced breast feeding, excessive alcohol intake, and postmenopausal obesity, all increase risk. Estimates suggest that 34% of breast cancers could be eliminated by lifestyle changes at the time of menopause. (Sprague BL. Et al. Proportion of invasive breast cancer attributable to risk factors modifiable after menopause. Am J Epidemiol 2008; 168(4):404-11)

Menopausal Women Seeking Relief from Complementary and Alternative Medicine

- Recent systematic review of complementary and alternative therapies (CAM) for treatment of menopausal symptoms reports that “Although individual trials suggest benefits from certain therapies, data are insufficient to support the effectiveness of any complementary and alternative therapy in the management of menopausal symptoms.” (Nedrow et al. Arch Intern Med 2006; 166(14): 1453-1465)

How Attitudes to Hormone Therapy Have Changed in the Past Decade

In the 1990s – The best medical advice was that hormone therapy would improve the quality of life for menopausal women (e.g. fewer hot flashes, somatic pains better sleep, less irritability and mood swings), reduce osteoporosis and cardio-vascular disease, with a small impact on breast cancer risk)

In 2009 – What the SOGC Update says:

- Nothing is as effective as hormone therapy for vasomotor symptoms and most complementary and alternative medicine act as placebos
- Hormone therapy will relieve joint pain and prevent bone loss when used for vasomotor symptoms
- Systemic hormone therapy may, and intra-vaginal estrogen will, relieve urogenital atrophy
- Hormone therapy used early in menopause does not increase the risk of coronary artery disease and used for five years or less has little appreciable effect on breast cancer risk

Management of Moderate to Severe Menopausal Hot Flashes – Update 2009

- Hot flashes is a vasomotor symptom of menopause, and is the primary indication for **hormone therapy**, the most effective treatment
- It is highly effective for the prevention of bone loss and osteoporotic fractures while being used for treatment of hot flashes
- HT is often sufficient to relieve urogenital atrophy and vaginal dryness as well
- Quality of life must be balanced against potential risks. An individualized assessment of risks is needed. Any prescription of HT requires a discussion of potential risks and benefits and these must be put into absolute numbers (not percentages) to place them into context
- If hot flashes are mild and not distressing, **lifestyle choices** may reduce the frequency and severity of symptoms
- For moderate to severe vasomotor symptoms, **complementary medicines** are not recommended
- If hormone therapy is unacceptable, serotonin-norepinephrine reuptake inhibitors (SNRIs) may be tried
- Other **non-hormonal therapies** may be tried: e.g. gabapentin, clonidine, bellergal

Hormone Therapy and Risk of Breast Cancer – Update 2009

- Breast cancer remains the number one worry of women considering hormone therapy
- According to the WHI study:
 - There was no increased risk of breast cancer in first-time HT users if used for four years or less
 - Before WHI, only 3% of estrogen/progestin users in the US continued use for more than five years
 - Overall breast cancer risk increased by 26% after four years of estrogen/progestin use. This translates into an increase of eight additional cases per 10,000 women, per year. According to the **World Health Organization and the Council for International Organizations of Medical Sciences** classification of adverse events, a risk of < 1 per 1000 is considered 'RARE'
- The Update says that when menopausal women present with distressing vasomotor symptoms, they can be reassured that short term use (less than five years) of either combined estrogen/progestin or estrogen alone will have little appreciable effect on their personal breast cancer risk
- The Update says that longer term HT use increases risk to a level similar to risks that many women accept such as daily alcohol ingestion, lack of regular exercise and postmenopausal obesity
- Population changes have contributed to rising breast cancer incidence (e.g. later first pregnancy and less breast feeding, obesity). "Breast cancer incidence would be reduced in half from 6.3/100 to 2.7/100 if women had the average number of births and lifetime duration of breast feeding that had been prevalent in developing countries until recently." **Collaborative Group on Hormonal Factors and Breast Cancer. Breastfeeding. Lancet 2002; 360:187-195**
- Analysis of modifiable risk factors that could be altered after menopause has been reached suggests that "a substantial fraction of postmenopausal breast cancers (34%) may be avoided by purposeful changes in

lifestyle later in life.” (Sprague BL. Et al. Proportion of invasive breast cancer attributable to risk factors modifiable after menopause. Am J Epidemiol 2008; 168(4):404-11)

- A recent comprehensive analysis of breast cancer news in leading media outlets found that articles on breast cancer risk factors tended to focus narrowly on pharmaceutical products, such as hormones, with little if any coverage of other equally important risk factors or preventive strategies related to lifestyle. (Atkin CK et al. A Comprehensive Analysis of Breast Cancer News Coverage in Leading Media Outlets Focusing on Environmental Risks and Prevention J Health Communication 2008; 13:3-19.)
- The impact of the media on public perception is important because research has shown that strong beliefs about risk, once formed, change very slowly and are extraordinarily persistent in the face of contrary evidence. (Vincent Convello, Centre for Risk Communication, Columbia University)

Hormone Therapy and Cardiovascular Disease in Women – Update 2009

- A definitive study on cardio-vascular disease benefits and risks is lacking. No randomized controlled trial has recruited sufficient numbers of newly menopausal women and followed them long term
Hormone therapy does not increase risk of cardio-vascular disease in newly menopausal women when started on HT within the first 10 years after menopause. “If women start hormone therapy within the first 10 years after the onset of menopause to treat hot flashes and night sweats, and remain on the hormones for no more than four to five years, they can take the fear of heart disease out of the question.” (Dr. Jacques Rossouw, lead author of WHI studies)
- Women with premature menopause may be less likely to develop cardio-vascular disease if maintained on HT until the usual age of menopause
- Healthy life choices and the use of established medications for cardio-vascular disease prevention should remain the mainstay of strategies to reduce cardio-vascular disease in Canada’s aging population

Hormone Therapy and Risk of Stroke - Update 2009

- There is conflicting data about the risk of stroke in HT-users
- WHI found an increased risk of ischemic stroke (blood supply to part of the brain is decreased, leading to dysfunction of the brain tissue in that area)
 - The absolute risk for the entire population was 0.8/1000 conjugated equine estrogen and 1.2/1000 woman-years conjugated equine estrogen/medroxyprogesterone acetate
 - 73% of women in WHI study were deemed to be at ‘medium-high’ risk for stroke (because they were obese , smokers, hypertensive), based on the Framingham scale
 - Aspirin used for heart attack prevention is associated with an absolute increase in the risk of hemorrhagic stroke of 12/10,000 individuals per year. Benefits are considered to outweigh the risks because there is a reduction of 137 heart attacks and 39 fewer ischemic strokes per 10,000 individuals per year.

Hormone Therapy and Risk of Venous Thromboembolism – Update 2009

Menopausal hormone therapy very slightly increases the risk of a blood clot (1-2 additional cases per 1,000 users)

- The risk decreases over time
- Age is greater risk factor:
 - 50-59
 - 60-69 risk doubles
 - 70-79 risk quadruples
- Weight
 - Overweight 1.96 (1.33-2.88)
 - Obese 3.09 (2.13-4.49)
- Risk is reduced with lower doses and transdermal (patches on the skin) HT

Hormone Therapy and Urogenital Atrophy – Update 2009

- Urogenital ageing results in symptoms such as bladder urgency and frequency, recurrent urinary tract infection, vaginal dryness, painful intercourse, and recurrent infection
- Systemic HT should be used when prescribed for control of vasomotor symptoms
- Local vaginal estrogen is highly effective for urogenital atrophy with minimal systemic absorption

Hormone Therapy, Estrogen and the Brain - Update 2009

- Estrogen has myriad actions in the brain interacting with neurotransmitters in mood, anxiety, memory and thermoregulation
- Mood disorders are among the most common symptoms of menopause and contributes to decreased quality of life
- Memory complaints are common in menopause
- There is conflicting evidence with respect to the impact of estrogen on cognition
- Timing may be everything: WHIMS studies show that estrogen can contribute to cognitive decline when given to *older* women (only those who had never had perimenopausal estrogen). There is some evidence that estrogen in *younger* menopausal women reduces the risk of later cognitive impairment.