Surviving Menopause
Without Systemic HRT

Christiane Kuntz, BA, MD, CCFP, FCFP

As presented at the University of Ottawa's
52nd Annual Refresher Course for Family Physicians
(November 2003)

Since the initial Women's Health Initiative (WHI) study findings were published in July 2002, hormone replacement therapy (HRT) has become a particularly hot topic for primary care providers.

A closer look at the WHI

It had been previously recommended that physicians prescribe estrogen and estrogen/progesterone combination therapy not only for symptom control, but also to protect patients from cardiovascular (CV) disease, osteoporosis, and dementia. However, some data suggested that systemic HRT, of the sort used in the WHI study, could potentially render more harm than good, particularly with prolonged use.

Calculating increased risk

In the WHI study, the increased absolute risk was calculated for each undesirable outcome, including coronary artery disease, stroke, pulmonary embolus, and invasive breast cancer. The calculated difference in absolute risk between treated and untreated study patients was found to be slightly < 1% over 10 years of use of these systemic hormones. However, when considering treatment of a large population of healthy menopausal women, the results become much more concerning.

It is important to keep in mind that one can only apply the WHI results to the older popula-

Joan's case

Joan, 47, presents with complaints of severe hot flashes, dyspareunia, insomnia, and mood swings. She became amenorrheic 13 months ago, following a three-year period of irregular bleeding and variable flow.

Family history includes a 37-year-old sister who died of breast cancer and a maternal aunt who developed the disease at age 42, but was treated and is still cancer-free at 68.

Joan is afraid to consider systemic hormonal replacement therapy for her problems. She has been using St. John's wort, but it has not been overly helpful in managing her depression.

What treatment options might you suggest to her?

For a followup on Joan, go to the next page.

tion of menopausal women (average age in the study being 63) taking continuous, combined treatment with conjugated equine estrogen, 0.625 mg per day, plus medroxyprogesterone, 2.5 mg per day (widely used HRT regimen in North America when the study was initiated).

Transdermal preparations are theoretically felt to be safer, since the dosages required to achieve the same clinical effect are lower. What is fascinating is that in a group of hysterectomized women (one arm of the WHI study) in which only conjugated equine estrogen, 0.625 mg per day, or placebo were being administered, similar increases in the risk of the previously described negative outcomes have not been shown except for stroke. Could progesterone be causing some of the perceived increase in risk? The study was intended to be completed in 2005.

Considering the sample population

Another big question is whether the results would have been different had the study group been composed primarily of newly menopausal women. The WHI study was not designed to evaluate the primary indication for HRT in present-day use (*i.e.*, for symptom control). Highly symptomatic women were excluded from the study. Some preliminary data and some reanalysis of the WHI data suggests that if you treat a healthy, younger woman with systemic HRT, there may be a protective effect seen for CV disease and dementia. This could explain the somewhat different results seen in some earlier studies, which led physicians to offer HRT for cardioprotection in the first place.

Coming up with alternatives

In light of the fact that patients are requiring and demanding alternatives to deal with the sometimes very severe symptoms of menopause, there needs

Dr. Kuntz is an assistant professor, department of family medicine, University of Ottawa, Ottawa, Ontario, and has a private family practice, Gloucester, Ontario.

A followup on Joan

For Joan's hot flashes, the most effective herbal remedy would likely be black cohosh. If Joan were interested in trying another option, you could recommend a serotonin norepinephrine reuptake inhibitor (SNRI) or a selective serotonin reuptake inhibitor (SSRI). However, before starting the SNRI/SSRI treatment, she must discontinue St. John's wort and be off it for at least a month. You could also recommend deep breathing exercises, regular exercise, keeping cool, wearing layers, reducing stress, and avoiding triggers. Gabapentin could be used for more severe symptoms.

For Joan's dyspareunia, you could suggest a trial of vaginal moisturizers or vaginal lubricants. Regular sexual activity would be helpful by promoting natural vaginal lubrication. If the problem of vaginal atrophy is so severe that Joan is uncomfortable having intercourse, suggest either an estradiol-impregnated ring or estradiol vaginal tablets.

Joan's insomnia and mood disturbances might also improve with the use of SNRIs or SSRIs. Teaching her good sleep hygiene techniques and recommending regular exercise could also be very helpful.

Finally, although Joan is very concerned about systemic HRT because of her family history of breast cancer, it would not be unreasonable to recommend short-term use for her various menopausal difficulties until the more severe symptoms have subsided. Transdermal preparations would likely be the best option.

to be other options. If the alternative treatments are not acceptable or not effective, each woman must decide whether an improved quality of life is worth the perceived risk of systemic HRT.

If a well-informed woman needs or desires HRT for symptom control, she should be treated at the lowest dose required for the shortest period of time with what are perceived to be the safest formulations.

What are the major symptoms/ issues in the menopause transition?

Irregular bleeding

Ninety per cent of women experience four to eight years of menstrual changes consisting primarily of oligomenorrhea/hypomenorrhea, menorrhagia/ metrorrhagia, sudden amenorrhea (12%), and perimenopausal bleeding. Treatment approaches are listed in Table 1.

Hot flashes

Eighty-five per cent of women experience this hallmark symptom of perimenopause. The flashes are an especially severe problem in surgically, chemotherapeutically, or radiation-induced menopause. Treatment options are listed in Table 2.

Sleep disturbances

One-third to one-half of women report sleep problems with insomnia and greater use of prescription sleeping aids, as well as sleep disorder-related breathing difficulties. Treatment involves discussion about sleep hygiene.

Vaginal atrophy

One-third of menopausal women have concerns about vaginal dryness. Treatment includes water-soluble lubricants and vaginal moisturizers. Encouraging regular sexual activity also helps by promoting natural lubrication. For more severe problems, localized estradiol treatment can be used. For this treatment, an estradiol-impregnated

Table 1

Treatments for irregular bleeding in perimenopausal women

Testing comes first

- Rule out organic causes; watch for anemia
- Consider doing transvaginal pelvic ultrasound
  - If lining is 5 mm or less following a bleed, no further concern regarding possible uterine cancer
  - If endometrial thickness > 5 mm, consider endometrial biopsy

Treatment options

- Trial of cyclic progesterone
- Contraceptive pills/patches/rings (for non-smokers)
- Tranexamic acid, 1 g orally four times daily, on first days of period
- NSAIDs may help dysmenorrhea and decrease menstrual flow
- GnRH agonists induce reversible hypoestrogenic state
- Danazol may decrease bleeding up to 80% (100-200 mg/day)
- D & C is not recommended unless required for biopsy
- Endometrial ablation/resection
- Uterine artery embolization for some fibroids
- Progesterone-impregnated IUD

NSAID: Non-steroidal anti-inflammatory drug
GnRH: Gonadotropin-releasing hormone
D & C: Dilatation and curettage
IUD: Intrauterine device

Table 2

Treatments for hot flashes in perimenopausal women

- Systemic estrogen: 80% efficacy
- Systemic progestin: 80% efficacy (not widely used)
- SSRI/SNRI: 50% efficacy
- Gabapentin: About 50% efficacy
- Deep breathing exercises: About 40% efficacy
- Placebo: Up to 40 % efficacy
- Clonidine: 30% efficacy
- Bellergal Spacetabs®: 30% efficacy
- Vitamin E (800 IU/day): Better than placebo; 10-20% efficacy
- Black cohosh: Better than placebo
- Red clover: May be more effective than placebo
- Evening primrose oil, soy proteins, dong quai, ginseng: No more effective than placebo
- Combination products: Inconclusive studies
- St. John's wort: Not studied in menopause; affects drug metabolism
- Chastetree: Not studied in menopause
- Kava: May be useful, can be hepatotoxic; not available in Canada

SSRI: Selective serotonin reuptake inhibitor
SNRI: Serotonin and norepinephrine reuptake inhibitor

ring is placed in the vagina for three months. The ring releases 5 mcg to 10 mcg of estradiol into the vaginal tissues per day. The ring is then replaced by the patient or the clinician. Patients are able to have intercourse with the ring in place. Alternatively, estradiol tablets, 25 mcg, are inserted about one-third of the way into the vagina with a tiny applicator every night for two weeks, and then twice weekly for as long as is required. These treatments do not have a systemic effect and are safe in patients who must avoid systemic estrogen treatment.

Urinary complaints

Ten per cent to 30% of women report urinary incontinence and recurrent urinary tract infections (UTIs). Treatment includes avoiding bladder irritants, avoiding fluid restriction, recommending good perineal hygiene practices, Kegel exercises, biofeedback, timed voiding, and anticholinergics. Surgery is a last resort. Cranberry juice can be used to decrease the risk of UTI.

Headaches

Eighteen per cent of women suffer from migraine, which may be aggravated by hormonal fluctuation. Post-menopausally, about two-thirds of women may experience remission of these headaches. The same treatments used in non-menopausal women would be helpful.

Mood fluctuations

Ten per cent of perimenopausal women have reported mood fluctuations in long-term, community-based studies. Treatments include selective serotonin reuptake inhibitors and serotonin and norepinephrine reuptake inhibitors.

Decreased libido

Decreased libido is a complex problem involving hormonal, psychologic, and other physical factors. Treatment with testosterone is still controversial and not to be undertaken without the patient being on systemic estrogen therapy.

Skeletal system effects

Systemic estrogen therapy is no longer recommended as a first-line treatment for osteoporosis.

Bisphosphonates/SERMs should be considered, along with lifestyle recommendations such as :

- weight-bearing exercise,
- resistance training,
- adequate calcium (1500 mg/day) and vitamin D (400 IU/day to 1000 IU/day),
- avoidance of caffeine, alcohol, smoking, and medications that can be detrimental to bone health.

Cardiovascular effects

Systemic estrogen therapy is no longer indicated for primary or secondary prevention of heart disease. Studies are ongoing.

Weight gain

Average women gain about 2.25 kg during the perimenopause stage. This weight gain is not related to menopause or systemic HRT, but to aging and changes in lifestyle. Dx

Resource

1. Menopause Core Curriculum Study Guide, 2nd edition. Available through The North American Menopause Society.

Further references available—contact *The Canadian Journal of Diagnosis* at **diagnosis @sta.ca**.