



C-Gyn 16

Hormone Therapy Advice

Advice to Medical Practitioners regarding the use of postmenopausal hormone therapy

The purpose of this statement is to provide evidence-based advice for the medical community regarding Hormone Therapy (HT, otherwise called HRT or Hormone Replacement Therapy). In this statement, HT refers to the use of oestrogen alone and oestrogen plus progestin (progestogen) for the use of women around midlife.

HT is effective and may be used for:

- the management of some menopausal symptoms such as hot flushes, night sweats, sleep disturbance
- the treatment of vaginal atrophy and associated sexual problems
- the prevention of fragility (osteoporotic) fractures as an option when first line therapies are not available or are contraindicated

For otherwise healthy women with moderate to severe symptoms, the benefits of short term HT are likely to outweigh the risks.

Disease Prevention and Possible Risks of HT

The focus of this statement has been on using the best quality data available. In most instances, these have been from the Women's Health Initiative (WHI) study conducted in the USA. It should be noted that the participants in these chronic disease prevention studies were generally older than women conventionally treated for menopausal symptoms, and hence their risks for adverse events were generally higher. The WHI was not designed to address the short term risks and benefits of hormones given for the treatment of menopausal symptoms. The Women's International Study of long Duration Oestrogen after Menopause (WISDOM) was a randomised placebo control trial that included Australian and New Zealand women and studied symptom control and quality of life.

Disease risk estimates are given for Australian women around the age of 50 years. The possible changes in risk are provided directly from the WHI study of women aged 50-79 years. Data are not available for the possible long-term effects of HT in Australian women, or for women specifically in the early postmenopausal years. Thus, the figures from WHI provide the best available estimates of risk in the broad age group studied. It cannot be assumed that the same risk estimates apply to subgroups, for example, women aged 50-59.

Coronary Heart Disease

Coronary heart disease in healthy low risk women within the first 10 years of natural menopause is uncommon. The incidence of hospitalisation for the diagnosis of coronary heart disease for women aged 45-54 years is approximately 39 cases per 10,000 per year (AIHW National Hospital Morbidity Database). A significant increase in cardiovascular risk was only seen in WHI in women who commenced combined HRT after age 70. There is insufficient evidence regarding the effects of HT on Coronary Heart Disease in the early post-menopausal years. HT should not be initiated for the prevention or treatment of coronary heart disease. Oestrogen may prevent post menopausal coronary artery disease when commenced near

menopause but cannot reverse established calcification and artery thickening when HRT is commenced many years after menopause.

Venous Thromboembolic Events (VTE)

In healthy women with no risk factors for VTE, the risk increases substantially with age. The absolute baseline risk for women aged in their 50s is 1 in 10,000 per year, increasing to 100 per 10,000 per year for women aged in their 80s. The use of oral HT is associated with an approximate doubling of this risk. Women at high risk of VTE should be individually assessed if HT is being considered and non-oral routes preferred.

Stroke

Stroke is uncommon in women in the first decade after natural menopause, with the approximate incidence rate for women aged 45-54 years, based on a population study, being 7-8 strokes per 10,000 women per year. In women aged 55-64 this increases to 26 per 10,000 per year.

In the Women's Health Initiative Study, the use of HT by women aged range 50-79 years was associated with an increase in risk of stroke of approximately 8-12 events per 10,000 women per year.

Cognition and Dementia

Studies of HT on cognitive function do not show consistent effects. There is insufficient evidence at this time to indicate an increase or decrease in the risk of dementia with the use of HT.. HT should not be used for the prevention or treatment of dementia.

Osteoporosis and Fracture

HT reduces the risk of spine, hip and other fragility fracture. In asymptomatic post-menopausal women at risk, HT may be an option for reducing fracture risk when first line options are not available or are contraindicated. Information on the therapies for the prevention of fragility (osteoporotic) fracture can be found in: Seeman E. Eisman JA. *Treatment of osteoporosis: why, whom, when and how to treat. The single most important consideration is the individual's absolute risk of fracture* (MJA 2004; 180:298-303).

Breast Cancer

The risk of invasive breast cancer for women aged 50-59 years is approximately 27 per 10,000 women per year. The use of combined oestrogen-progestin therapy in the WHI study was associated with an increase in risk for women aged 50-79 years of approximately 8 extra cases per 10,000 women per year. Increased risk is associated with duration of exposure (in WHI, the increase in breast cancer became evident after 4 years of use). The only major randomised trial of oestrogen-only therapy in hysterectomised women (WHI) showed no increase in risk of invasive breast cancer after 6.8 years. Most level 3 observational studies do not show an increase in breast cancer risk with oestrogen-only therapy. There are no long-term data from randomised controlled trials beyond 7 years but observational data suggests that very long-term use of oestrogen-only therapy e.g. 10-20 years may be associated with an increased risk of breast cancer. There are insufficient data to know whether these effects differ with the type of oestrogen or progestin.

Ovarian Cancer

Some studies have suggested a possible increase in ovarian cancer with HT. However, there is insufficient evidence from high quality studies to draw conclusions regarding the effects of HT on ovarian cancer. The age standardised incidence of ovarian cancer in Australia for women aged 50-59 years was 1-2 cases per 10,000 women per year.

Endometrial Cancer

Endometrial cancer is diagnosed in approximately 4-5 women per 10,000, aged 50-59, per year in Australia. There is no increased incidence with continuous combined HT. Sequential regimens require adequate progestin or endometrial cancer risk may be increased. There is a well documented increase in risk associated with oestrogen-only therapy in women with an intact uterus.

Colorectal Cancer

Some studies have suggested a possible decrease in colorectal cancer with HT. However, there is insufficient evidence from high quality studies to draw conclusions regarding the effects of HT on colorectal cancer. Colorectal cancer is diagnosed in about 6-7 women per 10,000, aged 50-59 per year in Australia.

Quality of Life

The main indication for HT use is to ameliorate debilitating menopausal symptoms and improve quality of life. This was shown in WISDOM where compared to placebo HT improved vasomotor symptoms, sleeplessness, joint pains and vaginal dryness. Unscheduled bleeding, breast tenderness and vaginal discharge were more common with HT.

Special considerations:

Duration of Therapy

As the risk benefit ratio will change with time, all women should be reviewed at least annually. Notwithstanding the lack of quality evidence, the lowest effective dose should be prescribed. Some women may require long-term therapy for symptom control.

Early Menopause

There is no available evidence regarding the risks and benefits of long-term use of HT in women who undergo an early menopause. Based on expert opinion, women who have undergone an early menopause are usually advised to use HT until they reach the age of natural menopause.

Bio-identical Hormones

These products are not registered as medicines. There is no evidence either for the safety and efficacy of hormonal products described as "bio-identical" or compounded hormones. They are not recommended.

Complementary Therapies

To date no complementary/alternative medicine (CAM) or therapy has been shown to have better efficacy than the placebo effect normally seen in quality blinded trials of HT. The long-term safety of CAMs is unknown.

Conclusion

All post-menopausal women for whom HT use is being considered should be fully informed of the potential benefits and risks of HT use to them.

Useful Links

Doctors may read a comprehensive review of the literature on the NHMRC web site:
<http://www.nhmrc.gov.au/publications/synopses/wh34syn.htm>

References

1. MacLennan AH. HRT: A reappraisal of the risks and benefits, *MJA* 2007;186:1-4.
2. MacLennan AH. An Evidence-Based Review of Therapies at the Menopause. *International Journal of Evidence-Based Healthcare* 2009 in press.

Disclaimer

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