For decades, women approaching and experiencing menopause have been advised by their doctors and urged by extensive advertising campaigns to use hormone therapy to treat symptoms, like hot flashes and vaginal dryness, and to ward off age-related illness and conditions, like heart disease and wrinkles. With the release of results from the Women’s Health Initiative (WHI), women learned that although hormone therapy is effective for treating menopause symptoms, most of the other claims made for the drugs were not supported by the evidence, and serious health risks of menopause hormone therapy exist.

Ovarian cancer causes more deaths than any other cancer of the female reproductive system and is the leading cause of death from gynecologic cancer in the US. Questions about whether hormone therapy might increase women’s cancer risk - particularly breast and ovarian cancer - have been raised for some time. Before the WHI the concerns about ovarian cancer were based mostly on associations observed in women taking hormones. The results of this trial also show a possible connection, but still no definitive answer. These results are significant because they are the first from a large randomized trial of healthy women.

Launched in 1991, the WHI is set of clinical trials and an observational study, which together involve more than 161,000 generally healthy postmenopausal women. The clinical trials were designed to test the effects of postmenopausal hormone therapy, diet modification (low-fat diet), and calcium and vitamin D supplements on heart disease, fractures, and breast and colorectal cancer. The hormone trial included 27,000 women in two studies: the estrogen-plus-progestin study of women with a uterus and the estrogen-alone study of women without a uterus. Women were randomly assigned to either the hormone medication being studied or to placebo. The drugs tested in the WHI are the ones that were most commonly used for menopause hormone therapy in the United States.

The estrogen-plus-progestin arm was stopped in July 2002, earlier than planned, because investigators found that - of the risks and benefits being measured - the risks outweighed the benefits. The estrogen-alone arm was stopped in March 2004 when investigators determined that the drugs were having no effect on heart disease (an intended benefit), making the increased risks unacceptable for healthy volunteers.

In the trial, more ovarian cancer occurred
among women taking estrogen-plus-progestin therapy than among women taking placebos, but the number of women in the trial who got ovarian cancer was small so the effect may have been due to chance. Twenty women taking hormones got ovarian cancer compared to 12 women in the placebo group. This translates to 15 additional ovarian cancers per 100,000 women per year in women. However, the small number of cases means that the difference is not statistically significant. Researchers concluded that estrogen-plus-progestin therapy may increase the risk of ovarian cancer though they acknowledged that their findings were not conclusive.

**Other Studies of Hormone Therapy and Ovarian Cancer**

In many observational studies which have followed women who choose to take hormones and compared them with women who do not, hormone use at menopause has been associated with an increased risk of ovarian cancer. A 2007 analysis that pulled together results from previous studies found this to be true for both women taking estrogen-alone and those taking an estrogen-plus-progestin combination. Even though the risk to an individual woman might be low, because these drugs are widely used, the increased risk translates into thousands of affected women. For example, in the United Kingdom, the Million Women’s Study Collaborators have attributed use of HRT to 1300 additional ovarian cancers and 1000 additional deaths from the malignancy since 1991 in the UK.

**Increased Duration of Use Increases Risk of Ovarian Cancer**

A recent 25 year follow up of the Nurses’ Health Study found a significantly increased risk of ovarian cancer and long duration of estrogen HT use, regardless of current or past use status. Compared to women who never used HT, current use of HT had a 41 percent increased risk of developing ovarian cancer, while past use increased the risk by 52 percent. The increased risk decreases within three years of cessation. Duration of use was found to be of concern, but the effect of duration varies between studies. In one study, ovarian cancer risk and mortality was increased after 10 years of estrogen use and that the risk of dying from ovarian cancer doubled with use of estrogen for 10 or more years. Another study has shown that even a five year duration of use can increase risk of ovarian cancer.

**Deciding Whether to Use Hormone Therapy**

There is really no single answer to the question “should I or shouldn’t I take hormones?” Each woman must make the decision for herself, taking into account her medical history, preferences and concerns. Women who have previously had cancer and are facing the decision may be particularly concerned about the proven increase in breast cancer with use of estrogen-plus-progestin and the possible increase in ovarian cancer. Women with a family history of ovarian cancer may share similar concerns, and their decision is made even more challenging by the fact that there is very little information about whether there may be a cumulative effect on risk of family history and use of menopause hormone therapy.

Alleviating hot flashes, vaginal dryness and preventing fractures are proven benefits of hormone therapy. But there are non-hormonal drugs that have been shown to reduce the risk of fracture and that do not appear to have the risks of hormone therapy, and there are also non-drug alternatives for addressing these problems. The National Women’s Health Network recommends that women who are concerned about bone fracture and women who experience troublesome hot flashes or vaginal dryness try non-hormonal therapies as the first line of treatment. If a woman chooses hormones, we suggest she take the lowest dose that alleviates her symptoms for as short a time as possible.

**Contact Us**

The National Women’s Health Network is committed to ensuring that women have access to accurate, balanced information. For more information,
References


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