The National Women's Health Network

Menopause Hormone Therapy & Breast Cancer

FACT SHEET



Since the early 2000s, the use of menopausal hormone therapy has continued to decline after the initial findings of the Women's Health Initiative (WHI) showed an increased risk of breast cancer and serious cardiac events with the use of estrogen plus progestin. The decline in MHT has been paralleled by a concomitant decrease in breast cancer incidence rates. Following the release of WHI results, there was a sharp decline in breast cancer incidence rates in the U.S..[1,2] In numerous countries where HT was used frequently by women, breast cancer rates decreased coincident with changes in prescribing and HT use patterns. [3,4] Ten years later, the results of the WHI continue to be celebrated in the prevention of numerous new breast cancer cases worldwide.

Estrogen/progestin combination hormone therapy causes breast cancer

On July 9, 2002, officials from the National Institutes of Health announced that one form of hormone therapy (HT), Prempro, was found to cause breast cancer in previously healthy women. These women were volunteer participants in the Women's Health Initiative, the largest and longest trial ever of estrogen therapy (ET) and HT. The WHI began in 1991 as the first randomized clinical trial to look at the long-term health effects of post menopausal hormone therapy. Just over 16,000 women participated in this section of the trial. Half of the trail participants were given an estrogen/progestin combination in the form of Prempro, and the other half was given a look-alike placebo with no active ingredients. Prempro is a combination of a synthetic estrogen (conjugated estrogen - Premarin) with a progestin (medroxyprogesterone - Provera).

By the time the trial was stopped, women had been taking their pills for an average of 5.2 years each. During that time, 166 women taking the hormone combination developed invasive breast cancer, compared to 124 women on placebo, an overall increase of 26 percent.[5] Another way of expressing the increased risk caused by Prempro is that each year, among 10,000 postmenopausal women taking estrogen/progestin, eight more will have invasive breast cancer. This increased risk of breast cancer does not appear until the hormones have been taken for at least two years. It also appears that the risk continues to increase with longer use.

Although the finding of increased risks halted the official study, participants continued to be monitored for long term effects of HT on the risk of developing breast cancer and other health problems. Therefore, the conclusions of the trial have been updated several times. In October

2010, after 11 years of follow-up, it was determined that combined estrogen/progestin HT increased the risk of dying from breast cancer from 1.3 deaths per 10,000 women per year to 2.6 deaths per 10,000 women per year, solidifying the concerns for the long term effects of HT.[6]

What about estrogen alone?

Another trial within the Women's Health Initiative studied a group of more than 10,000 women, all of whom had hysterectomies and took an estrogen therapy called Premarin. This ET study ended in 2004 after participants were found to have negligible prevention against heart disease and an increased risk of stroke. After seven years of evaluation, the trial found no increased risk of breast cancer. Instead, it found a decreased but statistically insignificant risk of breast cancer.[7] Interestingly enough, after 10 years of extended follow up, this decreased risk became statistically significant.[8] This recent analysis indicated that there would be eight fewer cases of breast cancer for every 10,000 women who had had a hysterectomy if they took estrogen daily for 6 years. These WHI findings differ from many other studies that find a positive correlation between estrogen therapy and an increased risk of breast cancer.[9,10,11,12] Biologically, estrogen may cause a proliferation of normal and malignant breast cells.[13] Observational studies with women using estrogen therapy for more than five years have found a 20 to 30 percent increased risk of breast cancer.[14] The Million Women Study found an increased incidence of breast cancer in current users of estrogen therapy, and greater risk for those using combined HT.[15] Some researchers argue that observational studies aren't as definitive as randomized controlled trials, but well conducted observational studies can be valuable and in several observational studies have correctly predicted increased breast cancer risk among women using combined HT. It is possible to explain the differences between the WHI findings and other observational study's findings due to differences in study design or other factors that may play a role in how estrogen affects breast cells, such as the study participants' ages, body masses and the preconditioning of breast cells to estrogen exposure.

Understanding menopause hormone therapy

Research on better and safer hormone therapy for menopause symptoms is constantly being generated. A new SERM type drug (bazedoxifene) and estrogen combination is currently under clinical review by the FDA for treatment of menopausal vasomotor symptoms and vaginal atrophy.[16] However, women will have to wait until long term studies are done to know if this or any other new drug increases the risk of breast cancer, stroke or heart disease since the FDA only requires studies of two to three months to approve new drugs to treat hot flashes. Steroid administration is also under consideration as an alternative to HT. Tibolone, a synthetic steroid, is used in over 90 countries to treat menopausal vasomotor symptoms and improve bone density. However, Tibolone is not approved for use in the United States. While evidence on Tibolone's risk for increasing the incidence of breast cancer is conflicting, it is currently contraindicated for use in breast cancer survivors, as Tibolone may lead to a relapse of breast cancer.[17] Another hormone, testosterone, commonly known as the male hormone, is being tested to alleviate common menopausal complaints.[18] The safety of testosterone has not been established. Among the concerns is the risk of breast cancer, since testosterone can be converted by a process known as aromatization into estrogen.[19] Acne and facial hair growth are other side effects of testosterone.

Are other forms of hormone therapy safe?

Although many other versions of hormone therapy exist, none have been put to the test of a long-term randomized trial such as the Women's Health Initiative. While it is possible that some form of hormones or hormone combinations may not increase the risk of breast cancer, the existing evidence suggests otherwise. Until proven otherwise through long-term randomized trials, we believe that women should assume that long-term use

of hormone therapy increases breast cancer risk.

During the last several years, newer forms of therapy, called selective estrogen receptor modifiers (SERMs), have become available. These drugs mimic some of estrogen's effects and have been used to treat hormone-sensitive breast cancers. Pharmaceutical companies hope to create a SERM that will help relieve hot flashes and vaginal dryness and prevent osteoporosis, heart disease and Alzheimer's without increasing the risk of cancer or blood clots.

Thus far, companies have successfully created a SERM that reduces the risk of bone fracture without increasing the short term risk of breast cancer.

Raloxifene (Evista) has been found to lower the risk of developing breast cancer in postmenopausal women by more than 70 percent. It has also been effective in preventing and treating osteoporosis and verterbral fractures.[20] In 2007, the FDA approved Raloxifene for treating and preventing osteoporosis in postmenopausal women and reducing the risk of invasive breast cancer in postmenopausal women who are at an increased risk of breast cancer.[21] However, raloxifene was also found to increase the incidence of blood clots and hot flashes.

Tamoxifen was the first SERM on the market and has been used by breast cancer survivors for decades. While Tamoxifen can decrease the risk of breast cancer during use, it also significantly increases the risk of blood clots, stroke and uterine cancer. The Network believes that Tamoxifen is too risky for most healthy women to use.

Conclusion

One of the many lessons learned from the Women's Health Initiative trials is to approach hormone therapy with caution. Research on HT is an ongoing process. While the search for definitive answers about the long-term health effects of other forms of HT continues, the Network recommends that women consider menopause HT as a last resort for short-term symptom relief rather than a tool for long-term health maintenance. To repeat the history prior to the Women's Health Initiative and use hormones for a purpose that has not yet been validated, is the last thing women want and need in order to protect their health.

Resources

If you would like to join with thousands of individuals in order to advocate for better treatment and access to care, contact the National Breast Cancer Coalition. To find out more about the activities of groups working on a national level to address the causes of breast cancer, including environmental connections, contact Breast Cancer Action, and the Breast Cancer Fund.

Contact Us

The National Women's Health Network is committed to ensuring that women have access to accurate, balanced information. For more information, email us at healthquestions@nwhn.org or call the Women's Health Voice at (202) 682-2646. Stay informed, connect with us on Facebook and Twitter.

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Updated: 2015