HRT Prescribing – Weighing the Evidence

20th August 2003

Breast cancer and the Million Women Study was published in the Lancet on August 9th 2003 and generated significant media interest.

What does the study tell us?

This study found that women taking any HRT have an increased incidence of developing breast cancer.

It confirms the findings of the Collaborative Group (1997) and the Women's Health Initiative (2002). It also confirms that the risk increases with increased duration of use.

Over 1 million women aged 50-64 were recruited in the UK between 1996 and 2001. More than 800,000 of these women were postmenopausal. 50% of the women had used HRT at some time. Of these, 50% had used combined oestrogen-progestogen preparations, 41% oestrogen-only preparations and 6% had used tibolone.

All women were followed up for cancer incidence and death. There were 9364 invasive breast cancers and 637 deaths from breast cancer in the follow up period.

The study also provides useful new information on different types of HRT. While all HRT use is associated with an increased risk, combined HRT (oestrogen-progestogen preparations) have a substantially higher risk than either oestrogen-only HRT or tibolone. Tibolone has similar relative risks to oestrogen alone. The risk is not affected by the type of oestrogen, the type of progestogen or the route of administration.

The risk of breast cancer in those who have used HRT in the past (once they had ceased to use HRT for more than one year) did not differ significantly from that of women who had never used HRT. The duration of previous use of HRT did not affect risk of developing breast cancer.

Absolute risks

It can be quite challenging to explain the concept of relative risk to our patients. Sometimes absolute numbers provide more useful information.

In women who have never used HRT, **32 women in every 1,000** will develop breast cancer between the ages of 50 and 65.

5 years of use of **oestrogen-only** HRT beginning at age 50 results in **1.5** additional breast cancers by age 65 in 1,000 users.

5 years of use of **combined HRT** beginning at age 50 results in **6** additional breast cancers by age 65 in 1,000 users.

10 years use of **oestrogen-only HRT** from age 50 is estimated to cause **5** additional breast cancers

10 years use of **combined HRT** from age 50 is estimated to cause **19** additional breast cancers

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What advice should we give our patients?

- There is no need for urgent treatment changes. Women who are already taking HRT can be advised that there is no immediate danger and that they can continue using their current preparation until they are due for review by their prescribing doctor.
- GPs should arrange to review their patients on HRT at six monthly intervals.
- The decision whether to start or continue HRT must be an individual one – with a careful weighing of the risks and benefits being discussed between each woman and her GP.
- Women who choose to stop their HRT immediately will do themselves no harm but should be encouraged to discuss their risk of osteoporosis with their GP subsequently.

For women considering HRT

- HRT is still the most effective treatment for the symptoms of the menopause.
- Relatively short-term use of HRT for symptom relief (probably up to 1 year) is associated with the lowest risk of breast cancer.
- Even short-term use of combined preparations appears to be associated with an increased risk of cardiovascular disease. (WHI study in NEJM, August 7th 2003)
- There are no apparent differences in risk profile of different oestrogens, different progestogens or different routes of administration.
- Oestrogen-only preparations and tibolone increase the risk of breast cancer significantly less than combined oestrogen-progestogen preparations.
- Because the increased risk of endometrial cancer with unopposed oestrogen is lower than the increased risk of breast cancer with combined preparations, oestrogen-only may be considered in the short-term for symptom relief in women with an intact uterus in the future. ***Please note that this approach goes outside the current license for oestrogen-only preparation.***
- There appears to be little indication for long-term use of HRT in the prevention of disease, with the exception of osteoporosis.
- Women with significant risk factors for osteoporosis should be carefully evaluated and all options, including HRT, should be discussed with them.

For current users

- Duration of use, indications for continuing use and risk profile should be carefully considered at each review.
- Women who choose to continue HRT in the longer term should have the risks and continuing benefits clearly outlined to them.
- Postmenopausal women who have an indication for continuing treatment should consider options such as tibolone or SERMS. Long-term use of tibolone increases the risk of breast cancer but the increased risk is approximately one quarter that of combined preparations.
- This study does not address the specific risk of breast cancer with long-term use of HRT in young women who have had a premature or surgically-induced menopause.

For past users

- Women who have taken HRT in the past can be reassured that their risk of breast cancer quickly returns to that of women who have never taken HRT quite quickly after stopping.
- Their duration of use of HRT does not influence their subsequent risk of breast cancer once they have stopped HRT.

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