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Ch. Jamin

TREATMENT OF MENOPAUSE AND BREAST IN PRACTICE

INTRODUCTION

Breast cancer is a major socio-economic problem, because one woman out of 10 could develop a breast cancer which is not only a threat for her life, but also for her appearance and her femaleness [1].

Recently there are approx. 60 articles concerning clinical studies about breast cancer risk and hormone replacement therapy, 1/3 with increasing risk, 1/3 with no risk modification and 1/3 with decreasing risk. It has to be noted that the most recent studies seem to show a light increase in the risk of detecting breast cancer in women with hormone replacement therapy (HRT) [2–6]. Recently two opinions seem to appear: first the risk might increase with the duration of HRT, and second the combination of estrogens and progestagens seems to be more deleterious than estrogens alone [2, 7–13]. These studies are epidemiological studies and no randomized clinical studies, therefore the consideration of biases is of great importance. The levels of relative risk (RR) which vary from 1.1 to 1.8 depending on the used HRT-regimens are not considered as reliable by biostatistical specialists. For them RR-levels of 3 or higher are reliable.

WHAT COULD DATA TELL US?

For example, a woman with HRT has a RR of 1.2 to develop a breast cancer. Until 5 years of therapy the RR will not increase. If the HRT is given for more than 10 years, the RR decreases up to 1.6. Some authors, who are in favour of an RR increase, try to compare this effect with the well-known results of the increasing risk of the duration of ovarian activity.

However there are two major problems interpreting these results: women with HRT cannot be compared with women without HRT, which has been known for years and proven by clinical prospective studies. Women with HRT have regular checks at their gynaecologist with breast examination and/or mammography. Depending on the study women with HRT have 15–40 % more mammographies than women without HRT. This may explain in part why breast cancer mortality is 30 % lower in women with HRT at the time of cancer detection [14–18].

RISK INCREASE AND DURATION OF THERAPY

In general the risk of detecting breast cancer is higher between the age of 60 and 65, corresponding to a duration of 10 to 15 years after menopause, which means 10 to 15 years of HRT. The potentially higher risk of developing breast cancer with HRT will appear 10 to 15 years later and could be suspended by improved screening. The effect of treatment duration and the effect of age will be intermingled.

COMBINATION THERAPY AND BREAST CANCER RISK

Concerning this point the publications are also contradictory, but there may be a tendency to increasing risk of breast cancer in women taking a combination of estrogens/progestagens than taking estrogens alone. Data for the combination therapy are not very convincing. Particularly in the Schairer study [11, 12] only 4 % of women with breast cancer were treated with a estrogen/progestagen therapy, 50 % got no HRT and 46 % were treated with estrogens alone. Considering the rare prescription of progestagens in the USA, one wonders why this 4 % of women got a combination treatment. No recent study is giving an answer to this question. Women taking progestins are those who are at risk of endometrial cancer and it is well known that women with endometrial cancer risk have also breast cancer risk.

Other, more indirect reasons are suggested recently to provide the theory of increased breast cancer risk under HRT, for example the increase of mastodynia with estrogen/progestagen therapy compared with estrogen alone, as it has been shown by the PEPI trial. There exists no evidence today that mastodynia induced by HRT is correlated to breast cancer risk. It has been considered that the density of mammary tissue is more increasing under combination therapy than with estrogen alone and even more without treatment. But there is also no evidence that increased mammographic density with HRT is correlated to higher breast cancer risk. In the PEPI trial this increase disappeared after one year of treatment.

However the anxiety of breast cancer in the general population and in some colleagues has to be considered: the prescription of HRT to women who are afraid of breast cancer should be avoided, because of lacking compliance.

TIBOLONE

This particular substance does not induce any increase in mastodynia or mammographic density. In experimental studies a decrease of estrogen synthesis in mammary tissue could be shown which is an important observation because all estrogens in breast tissue are not from circulating estrogens, but from *in situ*-synthesis.

Tibolone acts against the formation of estrone-sulphate into estrone and of estrone into estradiol. It also promotes the conversion of estradiol into estrone and estradiol-sulphate. Thus it is likely to have an anti-estrogenic effect by acting in the synthesis at the mammary level. In experimental models tibolone is associated with decrease of carcinogenesis inducted by DMPA at the breast level and with an deceleration effect of tumour growth in pre-existing tumours. An increase of breast cell apoptosis has also been observed. Although the current data in this field are very promising [19–23] more research is still needed.

Raloxifen

Like tamoxifen, raloxifen belongs to the SERM (selective estrogen receptor modulators) family. In a large randomised placebo-controlled study over 4 years (MORE trial) evaluating the effects of raloxifen on bone there could be reported a decreasing risk of breast cancer of almost 90 % in the treated women compared to those with placebo. This results in conjunction with good preventive results of tamoxifen has lead to statements that raloxifen could represent a treatment of osteoporosis risk in association with breast cancer prevention. This statements has to be regarded with caution because the duration of the study was not long enough and the substance can not be associated with inhibition of carcinogenesis, but with deceleration of pre-existing cancers' growth. Furthermore only differentiated forms (estrogen-receptor positive, ER+) are diminished, whereas the incidence of ER– breast cancers is not modified by treatment with raloxifen. The question is whether raloxifen simply slows down the development of estrogen-dependent clones without modifying the final incidence or prognosis of these cancers. Raloxifen could be prescribed for women with breast cancer risk, but without safety evidence [24].

Phytoestrogenes

In epidemiological trials it has been shown that life-long consumption of phytoestrogens is associated with a decreased risk of breast cancer detection, but it is just an association and not a causality factor. The increased consumption of phytoestrogens goes along with fewer saturated fatty acids consumption, which is considered to be correlated to breast cancer risk. It is thus impossible to decide if it is the increase of phytoestrogen-consumption or the decrease of fat consumption which is responsible for this decrease of breast cancer incidence, if there is a relationship between one of these factors and the disease. And nobody knows at which age and which duration – if any effect exists – it has to be looked for. Today phytoestrogens are prescribed to women, who are afraid of HRT because of breast cancer risk or because of a pre-existing breast cancer, but this is not based on any clinical study.

Conclusion

Thus the three substances – tibolone, raloxifen and phytoestrogens – are interesting for the treatment of some menopause symptoms for women with breast cancer risk or particularly afraid of breast cancer. As for now these are only theoretical hypothesis which have to be supported by long-term and difficult to obtaining studies [25, 26]. Finally it is important to mention that neither tibolone nor raloxifen should be used in women with breast cancer history.

References:

1. Feuer EJ, Wum L-M, Boring CC, et al. The lifetime risk of developing breast cancer. J Natl Cancer Inst 1993; 85: 892–7.

2. Collaborative Group on Hormonal factors in Breast Cancer. Breast cancer and hormone replacement therapy: collaborative reanalysis of data frome 51 epidemiological studies of 52 705 women with breast cancer and 108 411 women without breast cancer. Lancet 1997; 350: 1047–59.

3. Ettinger B, Quesenberry C, Schroeder DA, Friedman G. Long-term postmenopausal estrogen therapy may be associated with increased risk of breast cancer: a cohort study. Menopause 1997; 4: 125.

4. Persson I, Thurfjell E, Bergstrom R, Holmberg L. Hormone replacement therapy and the risk of breast cancer. Nested case-control study in a cohort of Swedish women attending mammography screening. Int J Cancer 1997; 72: 758–61.

5. Ross R, et al. Effect of hormone replacement therapy on breast cancer risk: estrogen versus estrogen plus progestin. J Natl Cancer Inst 2000; 92: 328–32.

6. Colditz GA, Egan KM, Stampfer MJ. Hormone replacement therapy and risk of breast cancer. Results from epidemiologic studies. Am J Obstet Gynecol 1993; 1473–80.

7. Colditz GA, Hankinson SE, Hunter DJ, et al. The use of estrogens and progestins and the risk of breast cancer in postmenopausal women. N Engl J Med 1995; 332: 1589–93.

8. Gambrell RD, Maier RC, Sanders BI. Decreased incidence of breast cancer in postmenopausal estrogen-progestogen users. Obstet Gynecol 1983; 62: 435–43.

9. Magnusson C, et al. Breast-cancer risk following long-term oestrogen and oestrogen-progestin replacement therapy. Int J Cancer 1999; 81: 339–44.

10. Nachtigall MJ, Smilen SW, Nachtigall RAD, Nachtigall LI. Incidence of breast cancer in a 22 year study of women receiving estrogen-progestin replacement therapy. Obstet Gynecol 1992; 80: 827–30.

11. Schairer C, Byrne C, Keyl PM, et al. Menopausal estrogen and estrogen-progestin replacement therapy and risk of breast cancer (United States). Cancer Causes Control 1994; 5: 491–500.

12. Schairer C, et al. Menopausal estrogen and estrogen progestin replacement therapy and breast cancer risk. JAMA 2000; 283: 485–91.

13. Stanford JL, Weiss NS, Voigt LF, et al. Combined estrogen and progestin hormone replacement therapy in relation to risk of breast cancer in middle-aged women. JAMA 1995; 274: 137–42.

14. Bergkvist L, Adami H-O, Bergstrom R, Krusemo UB. Prognosis after breast cancer diagnosis in women exposed to estrogen

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