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Invited Editorial

Menopausal hormone therapy and breast cancer risk: All progestogens are not the same

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Menopausal hormone therapy (MHT) is the treatment of choice for the management of bothersome menopausal symptoms, for the treatment of urogenital atrophy and for the prevention of osteoporotic fractures in symptomatic women at risk [1]. If given during the menopausal transition or soon after menopause, MHT may prevent cardiovascular disease [1]. Hormone replacement therapy (HRT), furthermore, should be administered to all women with premature ovarian insufficiency (POI) irrespective of the presence of menopausal symptoms, unless contra-indicated, for the prevention of chronic disease associated with premature estrogen decline [2]. The fear of breast cancer, however, deters many clinicians from prescribing MHT or HRT and makes women reluctant to receive it over the long term.

In this context, Vinogradova et al. [3] preformed a large case-control study using two large UK general practice databases with the objective to assess breast cancer risk associated with different types and durations of MHT. 98,611 women aged 50–79 with breast cancer were matched to 457,398 control women, based on age, general practice and index date. Estrogen-only therapy for up to 9 years increased only marginally the risk of breast cancer (OR 1.14, CI 1.08–1.21), whereas estrogen–progestin combination therapy for the same duration was associated with a more pronounced increase in breast cancer risk (OR 1.70, CI 1.64 to 1.76). The risk differed according to the progestin used, being higher with medroxyprogesterone acetate, levonorgestrel and norethisterone (OR 1.87 CI 1.71 to 2.05, 1.79 CI 1.68 to 1.90 and 1.88 CI 1.79 to 1.99 respectively) and lower with dydrogesterone (OR 1.24 CI 1.03 to 1.48) for more than 5 years of therapy. The excess risk dissipated in past users.

The study confirmed what we already knew from the WHI studies [4,5]: The excess risk of breast cancer associated with MHT is mainly conferred by the progestin. The risk presented in this study is lower than the risk published in a recent large meta-analysis [6]. The main message of this study, however, is that progestins do not exert a class effect on the breast. On the contrary, the risk of breast cancer varies between the various progestins used in MHT. Dydrogesterone-containing MHT regimens appear to have a lesser effect on the breast than medroxyprogesterone-, levonorgestrel- and norethisterone-containing MHT regimens. The findings of this study are in agreement with the results of the E3N study, a large prospective French cohort of 80,000 postmenopausal women followed up for a mean of 8 years. The risk of breast cancer varied significantly according to the progestogen used: the relative risk was 1.16 (CI 0.94–1.43) for estrogen–dydrogesterone and 1.69 (CI 1.50–1.91) for estrogen combined with other progestogens [7].

In conclusion, clinicians have to put the risk of breast cancer associated with MHT into clinical context: The risk associated with long-term estrogen use is much lower than the risk conferred by obesity, inactivity and alcohol use [8]. Furthermore, the findings of this study are not relevant to women with POI, in whom risks are calculated in comparison to women with regular menstruation. In general, tailoring hormone therapy to the needs of the individual woman ensures its long-term safety.

Contributors

Irene Lambrinoudaki is the sole author of this editorial.

Conflict of Interest

The author has no conflict of interest regarding the publication of this editorial.

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