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Type and timing of menopausal hormone therapy and breast cancer risk: individual participant meta-analysis of the worldwide epidemiological evidence

Collaborative Group on Hormonal Factors in Breast Cancer[‡]

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La Federación Latinoamericana de Sociedades de Climaterio y Menopausia (FLASCYM) solicitó al Presidente del Comité Científico Dr. Juan Enrique Blümel, sus conclusiones sobre el artículo publicado sobre THM y cáncer de Mama.

Dra. Zully Benítez Roa
Presidente FLASCYM 2019-2022

BACKGROUND: Published findings on breast cancer risk associated with different types of menopausal hormone therapy (MHT) are inconsistent, with limited information on long-term effects. We bring together the epidemiological evidence, published and unpublished, on these associations, and review the relevant randomised evidence. METHODS: Principal analyses used individual participant data from all eligible prospective studies that had sought information on the type and timing of MHT use; the main analyses are of individuals with complete information on this. Studies were identified by searching many formal and informal sources regularly from Jan 1, 1992, to Jan 1, 2018. Current users were included up to 5 years (mean 1·4 years) after last-reported MHT use. Logistic regression yielded adjusted risk ratios (RRs) comparing particular groups of MHT users versus never users. FINDINGS: During prospective follow-up, 108 647 postmenopausal women developed breast cancer at mean age 65 years (SD 7); 55 575 (51%) had used MHT. Among women with complete information, mean MHT duration was 10 years (SD 6) in current users and 7 years (SD 6) in past users, and mean age was 50 years (SD 5) at menopause and 50 years (SD 6) at starting MHT. Every MHT type, except vaginal oestrogens, was associated with excess breast cancer risks, which increased steadily with duration of use and were greater for oestrogen-progestagen than oestrogen-only preparations. Among current users, these excess risks were definite even during years 1-4 (oestrogen-progestagen RR 1·60, 95% CI 1·52-1·69; oestrogen-only RR 1·17, 1·10-1·26), and were twice as great during years 5-14 (oestrogen-progestagen RR 2·08, 2·02-2·15; oestrogen-only RR 1·33, 1·28-1·37). The oestrogen-progestagen risks during years 5-14 were greater with daily than with less frequent progestagen use (RR 2·30, 2·21-2·40 vs 1·93, 1·84-2·01; heterogeneity p<0·0001). For a given preparation, the RRs during years 5-14 of current use were much greater for oestrogen-receptor-positive tumours than for oestrogen-receptor-negative tumours, were similar for women starting MHT at ages 40-44, 45-49, 50-54, and 55-59 years, and were attenuated by starting after age 60 years or by adiposity (with little risk from oestrogen-only MHT in women who were obese). After ceasing MHT, some excess risk persisted for more than 10 years; its magnitude depended on the duration of previous use, with little excess following less than 1 year of MHT use. INTERPRETATION: If these associations are largely causal, then for women of average weight in developed countries, 5 years of MHT, starting at age 50 years, would increase breast cancer incidence at ages 50-69 years by about one in every 50 users of oestrogen plus daily progestagen preparations; one in every 70 users of oestrogen plus intermittent progestagen preparations; and one in every 200 users of oestrogen-only preparations. The corresponding excesses from 10 years of MHT would be about twice as great.

Comentario

Dr. Juan Enrique Blümel

El recientemente publicado estudio del Collaborative Group on Hormonal Factors in Breast Cancer, dirigido por la Dra. Beral, ha relacionado el uso de terapia hormonal de la menopausia con un mayor riesgo de cáncer de mama . Este análisis es un estudio caso-control anidado que no permite hablar de causalidad, sino que de asociación. Sin embargo, hay varios hechos que sugieren un rol de los estrógenos en el cáncer de mama. Por una parte, la menopausia precoz, un estado hipoestrogénico, se asocia a menos riesgos de cáncer de mama (RR 0.67; IC 95% 0.62-0.73) y, por otra parte, el uso de antiestrógenos es una efectiva terapia para tratar esta enfermedad . Igualmente, la menopausia, un estado obviamente hipoestrogénico, disminuye el riesgo de cánceres de mama agresivos . La THM provoca una pérdida de este efecto "protector" del hipoestrogenismo postmenopáusico y por ello sería plausible que la THM aumentara levemente el riesgo de cáncer de mama. Sin embargo, si ponemos en la balanza el positivo efecto de la THM en la calidad de vida y en el riesgo de enfermedades crónicas, el resultado es ampliamente favorable al uso de la THM. No hablemos más que el RR es un mal parámetro, este estudio menciona riesgos absolutos, o que las terapias actuales son diferentes a las terapias analizadas en esta publicación. Reconozcamos que pudiera haber algún nivel de riesgo con el uso de THM. No hay actividad humana que no implique riesgo, por ello los médicos que tratamos mujeres debiéramos trabajar con la hipótesis que la THM podría implicar un pequeño riesgo de cáncer de mama, hipótesis que el estudio de la Dra. Beral no prueba, pero que otros hechos, lo sugieren. ¿Dejaríamos de volar en avión porque existe la posibilidad de que éstos se caigan? No reconocer la existencia de riesgos en nuestras acciones diarias puede ser poco realista. No le pidamos a la THM lo que en el mundo real no existe. Pero, como en toda actividad humana, la relación costo beneficio es la que debiera guiar nuestra conducta médica.

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