probably involved heart disease). For the remaining causes, mortality in women with left sided tumours did not differ significantly from that in women with right sided tumours.

Most of the late cardiovascular deaths involved women treated for breast cancer in the 1970s, and improvements in radiotherapy techniques since then have tended to reduce radiation dose to the heart. For women treated in the 1980s, however, the cardiovascular ratio, left versus right, was still 1.11 but with a wide 95% confidence interval (0.95 to 1.29).

Comment

A mortality ratio, left versus right, of 1.10 for cardiovascular disease more than 10 years after diagnosis of breast cancer is compatible with a substantial hazard among some of those actually irradiated. For example, if about 30% of women surviving 10 years after breast cancer had been irradiated then a cardiovascular mortality ratio of 1.10 in all women and 1.00 in unirradiated women would suggest a ratio of 1.33 in those irradiated. This could be produced by a 60% increase in late cardiovascular mortality after irradiation for a left sided tumour and a 20% increase after irradiation for a right sided tumour. The confidence interval for the observed ratio of 1.10 is, however, wide, so the true cardiovascular hazard from radiotherapy in the 1970s and '80s remains uncertain.

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Drug points

Thromboembolism associated with the new contraceptive Yasmin

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Our centre, the Dutch spontaneous reporting system for adverse drug reactions, recently received five reports of thromboembolism as a suspected adverse drug reaction to the new oral contraceptive Yasmin (ethinylestradiol and drospirenone).

A 17 year old woman suddenly collapsed and died after taking the contraceptive for six months. Autopsy showed that she had had a massive pulmonary embolism. No obvious risk factors for thromboembolism, such as smoking, a period of long immobilisation, air flights, or concomitant medication, were evident.[1] Because she died suddenly no blood sample was taken. Blood taken from her parents did not test positive for any of the known risk factors: concentrations of protein C and antithrombin III were normal. The activated partial thromboplastin time and partial thromboplastin time were normal, and the existence of factor V Leiden mutation was excluded.

A 28 year old woman changed her oral contraceptive from ethinylestradiol with desogestrel (Marvelon) to ethinylestradiol with drospirenone. Four months later she had thrombosis in one leg and was treated with acenocoumarol. Risk factors or concomitant drugs were unknown.

Another patient, a 45 year old woman, had deep vein thrombosis in one leg after taking ethinylestradiol with drospirenone for two months, as did a 50 year old woman who took the contraceptive for three months. A 35 year old woman had pulmonary thrombosis 17 days after she started taking the contraceptive. She had given birth four months earlier.

Ethinylestradiol with drospirenone has been approved as an oral contraceptive in all European Union countries since 2000 and has recently been launched in the United Kingdom.[2] The public assessment report of the contraceptive gives only one suspected case of pulmonary embolism but also says that the number of cases in the preregistration studies are too low for a reliable conclusion on this matter.[3]

The risk of thromboembolism for women using the third generation (combined) pill has long been debated. Physicians therefore may prefer a new type of combined pill, like ethinylestradiol with drospirenone, assuming that these are safer. However, an association of these drugs with a lower risk of thromboembolism has not been proved by research, and our cases show that newer contraceptive pills may have a risk of thromboembolism. At present, insufficient data on the superiority of ethinylestradiol with drospirenone are available.

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