Letter

The protective side of progesterone

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See related commentary by Jerry, http://breast-cancer-research.com/content/9/2/102

According to Jerry's commentary [1], exogenous oestrogen and progesterone potently inhibit tumorigenesis, representing an interesting strategy to prevent breast cancer, but we feel that the concerns noted by Jerry deserve further comment.

According to the Million Women Study [2], when progesterone was included in the hormone replacement therapy (HRT) formulation, the odds ratio fell from 1.3 to 1.1, indicating a protective effect exerted by progesterone, though no significant difference in the relative risk of ovarian cancer was registered in the subgroups of women who used oestrogen only compared with those who used the combination. Long durations of use of unopposed oestrogen and of oestrogen plus progestin, especially sequential regimens, have been reported to be associated with increased ovarian cancer risk. In preclinical models, combined progestins circumvent the anti-apoptotic action of the long isoform of Fas-associating protein with death domain-like interleukin-1 beta-converting enzyme (FLICE)-like inhibitory protein, an anti-apoptosis mediator, representing an effective therapy for ovarian cancer cells [3]. In premenopausal women, combined oral contraceptives (OC) have been described to be effective at decreasing the risk of epithelial ovarian carcinoma, even though the strongest risk reduction has been associated either with low- or high-potency progestin formulations.

Some synthetic progestins, when added to oestrogen in HRT for menopausal symptoms, have been reported to increase the risk of breast cancer more than oestrogen alone. Progestin use in breast cancer survivors is associated with an increased breast cancer risk compared with its non-use [4]. However, outside pregnancy, progesterone endogenously produced or exogenously administered does not have a cancer-promoting effect on breast tissue. The greater breast cancer risk related to the use of HRT containing oestrogen and synthetic androgenic progestin (19-nortestosterone derivatives) could be due to the non-progesterone-like effects enhancing the oestrogen proliferative effect on oestrogen-sensitive cancer cells.

In postmenopausal women, progesterone is added to prevent the carcinogenic effect of oestrogen on the uterus [5]. In premenopausal women, the potency of the progestin in most OC appears adequate to provide a protective effect against endometrial cancer. Higher progestin-potency OC may be more protective than lower progestin potency OC among women with a larger body habitus. Progestagens counteract the adverse effect of oestrogens on the endometrium, the effect being greater the more days every month that they are added to oestrogen and the more obese that women are.

Finally, because hormones may play a crucial role in the development of breast, endometrial and ovarian cancer, the impact on cancer risk of progestins included in HRT or OC formulations remains a major interest.

Competing interests

The authors declare that they have no competing interests.

References

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FLICE = Fas-associating protein with death domain-like interleukin-1 beta-converting enzyme; HRT = hormone replacement therapy; OC = oral contraceptive.