

Percutaneous progesterone use and risk of breast cancer: results from a French cohort study of premenopausal women with benign breast disease.

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Percutaneous progesterone topically applied on the breast has been proposed and widely used in the relief of mastalgia and benign breast disease by numerous gynecologists and general practitioners. However, its chronic use has never been evaluated in relation to breast cancer risk. The association between percutaneous progesterone use and the risk of breast cancer was evaluated in a cohort study of 1150 premenopausal French women with benign breast disease diagnosed in two breast clinics between 1976 and 1979. The follow-up accumulated 12,462 person-years. Percutaneous progesterone had been prescribed to 58% of the women. There was no association between breast cancer risk and the use of percutaneous progesterone (RR = 0.8; 95% confidence interval 0.4-1.6). Although the combined treatment of oral progestogens with percutaneous progesterone significantly decreased the risk of breast cancer (RR = 0.5; 95% confidence interval 0.2-0.9) as compared with nonusers, there was no significant difference in the risk of breast cancer in percutaneous progesterone users versus nonusers among oral progestogen users. Taken together, these results suggest at least an absence of deleterious effects caused by percutaneous progesterone use in women with benign breast disease.

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Progestogen use and decreased risk of breast cancer in a cohort study of premenopausal women with benign breast disease.

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A cohort study of 1,150 premenopausal French women with benign breast disease diagnosed in two breast clinics between 1976 and 1979 was carried out to analyse the relationship between progestogen use and the risk of breast cancer. The follow-up accumulated 12,462 person-years. The risk of breast cancer was estimated using a Poisson regression analysis on person-time data and the proportional hazards model. In the latter analysis, cumulated progestogen use and age were considered as time-varying covariables and adjustment was performed on the main risk factors for breast cancer. Neither overall progestogen use nor the duration of use was found to be significantly associated with the risk of breast cancer. When progestogens were classified into two categories according to their hormonal potency (19-nortestosterone derivatives vs other progestogens), 19-nortestosterone derivative use was found to be significantly associated with a lower risk of breast cancer. In the adjusted model, the corresponding risk of breast cancer was 0.48 (95% confidence interval 0.25-0.90). In addition, there was a linear trend in the decrease of the relative risk of breast cancer with the duration of use ($P = 0.02$). These results do not support the hypothesis that progestogens might increase the breast cancer risk. They suggest, instead, that treatment with 19-nortestosterone derivatives might have a beneficial effect on the risk of breast cancer in women with benign breast disease.

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[The treatment of benign pathological conditions of the breasts with progesterone and progestogens. The results according to the type of breast condition (260 case records) (author's transl)]

[Article in French]

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This work reports the clinical results which were obtained after treating 260 women who had pathological conditions of the breasts using a combination of a progestogen which was given by a generalised route (orally or by injection) and progesterone which was applied locally so that its effect would be percutaneous on the breasts. These results were evaluated according to the effectiveness of the treatment according to the different symptoms or groups of clinical symptoms and radiological findings which had been noted at the time of the first examination. A better therapeutic effect was found in cases of early lesions where oedema was the dominant factor (mastodynia) and glandular hyperplasia (diffuse polyadenomatosis). On the other hand, longstanding lesions (sclerocystic mastopathia) where sclerosis was marked showed a much more variable result of treatment with progestogens. Therefore it seems that benign conditions of the breasts should be treated early and particularly in the stage of mastodynia if development into irreversible sclerotic conditions is to be avoided. It also has to be carried on for a long time, especially if there are other risk factors for cancer which are associated with conditions in the breast. The prophylactic role of this treatment in regard to cancer of the breast is discussed.

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Percutaneous administration of progesterone: blood levels and endometrial protection.

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There is controversy about the beneficial effects of topical progesterone creams used by postmenopausal women. A major concern is that serum progesterone levels achieved with progesterone creams are too low to have a secretory effect on the endometrium. However, antiproliferative effects on the endometrium have been demonstrated with progesterone creams when circulating levels of progesterone are low. Thus, effects of topical progesterone creams on the endometrium should not be based on serum progesterone levels, but on histologic examination of the endometrium. Despite the low serum progesterone levels achieved with the creams, salivary progesterone levels are very high, indicating that progesterone levels in serum do not necessarily reflect those in tissues. The mechanism by which the serum progesterone levels remain low is not known. However, one explanation is that after absorption through the skin, the lipophilic ingredients of creams, including progesterone, may have a preference for saturating the fatty layer below the dermis. Because there appears to be rapid uptake and release of steroids by red blood cells passing through capillaries, these cells may play an important role in transporting progesterone to salivary glands and other tissues. In contrast to progesterone creams, progesterone gels are water-soluble and appear to enter the microcirculation rapidly, thus giving rise to elevated serum progesterone levels with progesterone doses comparable to those used in creams.

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