erythrocytes. It is partly explained by acute phase increases in plasma fibrinogen concentration and viscosity. In particular, however, we found that the filterability of both polymorphonuclear and mononuclear leucocytes is reduced in acute cerebral infarction. This may not only explain the reduced filterability of blood but also promote malperfusion of the microcirculation and infarction.

Reduced filterability of leucocytes may be part of the acute phase response to injury, as suggested by the correlation with fibrinogen concentration in the patients with stroke and by similar findings in the controls with chest infection. Preceding infection is an important risk factor for cerebral infarction.[5] The risk of infarction also increases with age, and we observed decreased filterability of leucocytes in controls aged over 40. We suggest that mechanisms by which increasing age and infections increase the risk of cerebral infarction include increased plasma fibrinogen concentration and viscosity and decreased filterability of leucocytes, each of which tends to reduce capillary flow.

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Progesterone cream for cyclic breast pain

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Breast pain and nodularity during the luteal phase of the menstrual cycle may be due to insufficiency of progesterone. Local application of progesterone cream has been claimed to relieve these symptoms without affecting uterine function, but evidence that oral progesterone is effective is disputed. The use of progesterone cream for treating cyclic mastalgia has become popular in France after uncontrolled trials.[1] A randomised trial of cream (C Conti, unpublished data) gave sufficiently favourable results to justify further studies.

Patients, methods, and results

Women attending our breast clinic with cyclic breast pain of at least two months' duration were included in the study. Women not menstruating regularly, taking the contraceptive pill, or with breast abnormalities were excluded. The women were asked to record their pain on a linear analogue scale from one to 100 daily from the first day of menstruation.[2] The nodularity of the breasts was assessed by palpation on one day of the luteal phase of the cycle each month.

Patients who kept full records during a control month were randomised into the six month trial. They were asked to apply 5 g of cream each evening from the tenth day of one menstrual cycle to the first day of the next. Two different preparations in identical containers labelled first or second were used; one contained 1% natural progesterone and the other was without the active hormone. The active and placebo creams were applied for three months, each in random order, and only the statistician knew the order of the treatments. For each patient a mean pain score was calculated from the seven worst daily pain scores during the premenstrual phase each month. The seven worst days were usually consecutive and most often the days before the next period. The pain and nodularity scores for each patient were analysed by non-parametric tests, which compared differences within patients.

Thirty two women were entered into the study; 17 were randomised to use the active drug first and 15 the placebo. Seven did not return for their monthly appointments (usually after the first month). Thus complete data were available for 25 of the women, 14 of whom used the active treatment first and 11 the placebo.

The data were first analysed for trends in the pain and nodularity scores over time, but no evidence of any such trends was found. To compare the drugs a mean pain score and a total nodularity score were calculated for each patient's three month exposure to each drug.

Pain and nodularity scores in 25 patients with cyclic breast pain

Outcome	Median score	Median (95% confidence interval) difference (active-placebo)
Mean pain score at 3 months	44	3·3* (−3 to 12)
Total nodularity score over 3 months†	4	1·0* (0 to 1·5)

*Not significantly different from zero by Wilcoxon's signed rank test.
†Sum of three monthly ratings, each of which was scored 0=none, 1=slight, 2=mild, 3=severe.

The results (table) showed a small but non-significant benefit from the placebo over the active drug. The confidence intervals indicated that any difference between the two preparations was small.

Comment

We have found that progesterone cream applied locally was no better than placebo cream in relieving breast discomfort. Attempts to determine whether the cream was absorbed into the circulation by daily measurement of salivary hormone concentrations was unsuccessful; this was because the samples contained high concentrations, which we found to be the result of contamination from cream on the patients' fingers.

Many of the oral treatments for mastalgia—for example, bromocriptine, danazol, and tamoxifen—can have troublesome side effects,[3,4] and for a condition that can be self limiting their use is thus questionable.[5] A topical treatment would be preferable, but unfortunately we showed that progesterone had no effect.

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