possible benefits in a population with 700 000 births annually.

- If no one received any vitamin K 30-60 cases of late haemorrhagic disease might occur.
- If all received one dose of oral vitamin K 10 cases of late haemorrhagic disease might occur.
- If all received intramuscular vitamin K at most one case of late haemorrhagic disease might occur.

Conversely, calculation of the numbers of cancers that might be initiated is as follows. Assume that the incidence of cancer among those who did not receive vitamin K is 1·4 per 1000 by the age of 10 (data from the 1970 cohort study) and that the odds ratio for cancer if given intramuscular vitamin K is 2·0; then if intramuscular vitamin K is causally related:

- If no one received any vitamin K 980 cancers would occur.
- If all received oral vitamin K 980 cancers would occur.
- If all received intramuscular vitamin K 1960 cancers would occur.

The figures vary according to the assumptions made. If the estimate of the incidence of cancer in the absence of intramuscular vitamin K is higher then more cancers would be associated with intramuscular vitamin K. The balance appears approximately as follows:

- If no one received any vitamin K then there would be about 30-60 cases of late haemorrhagic disease and no extra cancers.
- If all received oral vitamin K there would be about 10 cases of late haemorrhagic disease and no extra cancers.
- If all received intramuscular vitamin K there would be one case of late haemorrhagic disease and 980 extra cancers.

Conclusion

It has always seemed physiologically perverse that evolution should have permitted the development of what is termed vitamin K deficiency in normal term infants who are breast fed, resulting in a small but definable risk of haemorrhagic disease of the newborn. The most likely explanation for this situation is that there is some evolutionary advantage that outweighs this risk. The finding of an increased incidence of childhood cancer in children given intramuscular vitamin K in the neonatal period suggests that a relative deficiency in vitamin K during this critical phase of rapid growth and development may protect vulnerable tissues from mutagenesis. The protection afforded by oral vitamin K against haemorrhagic disease does not appear to carry the same risk of inducing malignancy, so it may be prudent to use oral rather than intramuscular vitamin K.

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Fluoxetine treatment of severe premenstrual syndrome

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Premenstrual symptoms are common and may be disabling in 3-10% of women of reproductive age.[1] A link between the premenstrual syndrome and depression is suggested by symptom overlap and by the observation that pre-existing depression is often aggravated during the premenstruum.[2] The activity of brain serotonin systems, thought to have a role in the regulation of mood, seems blunted premenstrually.[3] It is thus surprising that so few attempts have been made to test the efficacy of serotonin enhancing antidepressants in the premenstrual syndrome.[4] We report a double blind, placebo controlled crossover trial of fluoxetine in severe premenstrual syndrome.

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Subjects, methods, and results

Subjects were selected from a community sample of 200 volunteers. Careful screening excluded those outside the age range 18-48, those taking regular psychotropics or diuretics or using hormonal contraception, and any with appreciable menstrual irregularity or psychiatric or substance use disorder. Samples of

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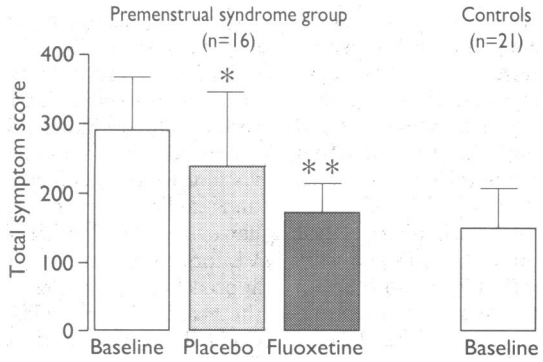
controls and women with presumptive premenstrual syndrome further agreed to self monitor premenstrual symptoms over three months with validated prospective and retrospective rating scales.[5] Diagnosis of the premenstrual syndrome requires recurrent severe symptoms and social or occupational impairment specific to the premenstruum. This was confirmed by daily ratings and by psychiatric interview in 21 women accepting the offer of a treatment trial. A sample of 21 age matched controls was chosen for comparison.

Subjects with the premenstrual syndrome were randomly assigned to begin fluoxetine 20 mg daily or placebo, continuing for three cycles before crossover. Self ratings were continued as during baseline. After each treatment phase subjects were reviewed independently by two blinded psychiatrists and global assessments made of treatment efficacy and tolerability.

The main measure of severity of the premenstrual syndrome was the total score on the premenstrual assessment form,[5] a monthly index of premenstrual change in 96 affective, physical and behavioural symptoms. Individual item scores ranged from 1 to 6. The total was distributed in an acceptably normal fashion. A within subjects repeated measures analysis of variance was used to assess treatment effect. Ordinal scaling was used for clinician rated efficacy and tolerability of treatment. These results were analysed by the Wilcoxon procedure.

Five women were excluded during the trial, two for protocol violation and three because of adverse effects of fluoxetine (two with intolerable nausea or insomnia, or both, one with rash and arthralgia). Of 16 women completing the trial, a good or very good response was seen in 15 given fluoxetine compared with three given placebo ($p<0{\cdot}01$). This effect was shown quantitatively by a striking reduction in symptoms of the premenstrual syndrome measured with the premenstrual assessment form (figure). Analysis of variance showed that the superiority of fluoxetine did not depend on whether it was given before or after placebo ($F_{1,14}=1{\cdot}75$; NS).



*Premenstrual assessment form score (mean and SD) after three months each of baseline, placebo, and fluoxetine treatment. Within subjects effect of treatment was significant ($F_{2,30}=19{\cdot}2$; $p<0{\cdot}001$). Mean (SD) symptom total from age matched control group completing three months of self rating shown for comparison. *$p<0{\cdot}05$ Compared with baseline. **$p<0{\cdot}01$ Compared with placebo*

The onset of action of fluoxetine was variable, seven of the 16 women showing improvement two weeks after initiation and eight responding after a further four to eight weeks. Prompt relapse of the premenstrual syndrome was observed 18-25 days after stopping fluoxetine in seven of nine women who crossed over to placebo, four rating their premenstrual syndrome as distinctly worse than usual. In women who chose to continue or resume fluoxetine after breaking the code efficacy was being maintained up to 12 months later.

Comment

Fluoxetine was an effective treatment for the severe premenstrual symptoms experienced by our sample, in 12 of 16 cases exceeding the effect of placebo. Patient enthusiasm for fluoxetine was clear, particularly among the eight women achieving full remission of symptoms. Several women expressed delight at feeling "normal" throughout their cycle, a view supported by the finding that while taking fluoxetine the premenstrual syndrome group had symptom scores comparable to those of a control sample (figure). The efficacy of fluoxetine in severe premenstrual syndrome was consistent with findings of other recent studies of serotoninergic agents, including buspirone, clomipramine, fenfluramine, and fluoxetine.[4] These results support the proposed role of serotoninergic hypoactivity in the aetiology of the premenstrual syndrome.[3]

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ONE HUNDRED YEARS AGO

SAVING LIFE AT FUNERALS

The Rev. F. Lawrence, Honorary Secretary of the Funeral Reform Association, writes to us to suggest that if the first part of the burial service is said where the departed has been in the habit of worshipping, attendance can be limited to this part of the funeral ceremony and all exposure to the cold avoided. Those who go to the grave can make use of a suitable hood or skullcap for the protection of the head, forehead, neck, and chest. Persons not using such a hood can raise their hats when the Holy Name is used and at the close of each prayer instead of remaining bareheaded the whole time. Officiating ministers in winter and when the weather is inclement can say the whole of the service in the church or cemetery chapel except the words of committal and the grace. Cemetery authorities can make the chapel warm and comfortable and provide an overhead canopy borne on four or more poles with tarpaulins on the weather side for the protection of mourners from wind and rain on their way to the grave, such canopy being convertible into a tent, which can be roughly planted at the grave-side.

(*BMJ* 1892;i:239)