

Premenstrual exacerbation of asthma

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ABSTRACT Questionnaires and twice daily peak expiratory flow measurements were used to evaluate the effects of the menstrual cycle in asthmatic women. Forty per cent of women reported premenstrual deterioration in their symptoms and this was confirmed by peak flow recordings. No correlations were found between premenstrual exacerbation of asthma and symptoms of premenstrual tension, consumption of aspirin, use of the contraceptive pill, cycle length, or behaviour of asthma during pregnancy.

Although premenstrual worsening of asthma is recognised,¹⁻³ little attention has been paid to the problem. In particular, little is known of the frequency with which it occurs, its severity, the relevance of medication such as analgesics or the contraceptive pill, or its relationship to other premenstrual symptoms. We have studied this phenomenon by means of a self administered questionnaire and by analysis of home peak flow recordings.

Patients and methods

One hundred and twenty six consecutive women aged 14-46 years attending an outpatient clinic for asthma were asked about variation of their asthma during the menstrual cycle. A questionnaire was then sent to the 114 women who had responded and it was returned by 91 of them. It included questions on the timing of any exacerbation in relation to menstruation, the frequency with which this occurred, and the perceived severity of the deterioration. The patients were also asked if they experienced any of the following premenstrual symptoms: headache, breast tenderness, stomach bloating, swollen ankles, nervous tension, irritability, depression, acne rash, or period pains; and the frequency of these symptoms was compared in the women with and without premenstrual asthma. We also enquired about the contraceptive pill and any drugs taken for premenstrual symptoms, and the effect of pregnancy on the severity of asthma was recorded.

Twenty one women who complained of premenstrual asthma and 12 who did not recorded their peak

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flow rate twice daily, using a mini Wright peak flow meter before bronchodilator treatment, for three consecutive months. We compared the mean morning and evening peak flow rates during the premenstrual week (the seven days preceding the menstrual period) and during the mid cycle week (days 10-16), using Student's *t* test.

Results

In response to the initial question "Has your asthma ever varied *with* your monthly period?" 49 patients (43%) answered "Yes" and 65 (57%) answered "No."

QUESTIONNAIRE RESULTS

When asked "Does your asthma ever seem worse *before* the menstrual period?" 36 patients (40%) answered "Yes" and 55 (60%) said "No." Most of the women had developed asthma in childhood and adolescence, but the mean age of onset of the premenstrual exacerbations was 25 (SD 8) years. The age of the women who complained of premenstrual worsening was not significantly different from those who did not.

Of those who experienced premenstrual asthma, 27 (75%) had it before most periods, seven (19%) before few periods (less than half), and two (6%) only once or twice a year.

Timing and severity of symptoms

In most patients the worsening occurred in the five days leading up to the period—in 15 one or two days before and in 14 three to five days; but in six cases it was five to 10 days and in one 10-15 days before the period.

Of the 91 women, seven regarded their asthma overall as being severe, 41 moderate, and 43 mild.

Table 1 Peak flow measurements in 21 women with premenstrual exacerbations of asthma (59 menstrual cycles)

Week	Mean (SD) peak flow ($l\ min^{-1}$)	
	Morning	Evening
Premenstrual	287 (108)	306 (112)
Mid cycle	303 (101)	317 (104)
<i>t</i>	2.750	2.408
Significance	$p = 0.01$	$p = 0.02$

All seven of the women who considered their asthma severe had premenstrual exacerbations, whereas only 14 (35%) of those with moderate asthma and 15 of those with mild asthma had premenstrual worsening. Fifteen patients perceived the premenstrual deterioration as mild, 14 as moderately severe, and seven as severe.

Relationships between premenstrual asthma and other factors

There was no correlation between premenstrual asthma and other premenstrual symptoms or use of aspirin. Approximately equal numbers of those with and without premenstrual asthma were taking the contraceptive pill and there was no effect of the pill on the overall control of the asthma. Thirty six women had had a total of 67 pregnancies. In 33 pregnancies the asthma had improved, in 14 it had deteriorated, and in 30 it had been unchanged. Seventeen patients had had more than one pregnancy and in 13 the asthma had behaved in a consistent way. The effect of pregnancy on asthma was not related to the occurrence of premenstrual asthma. There was no difference between menstrual cycle length in those with premenstrual asthma (mean 27.9 (SD 3.3) days) and those without premenstrual asthma (28.4 (3.2) days).

PEAK FLOW MEASUREMENTS

Fifty nine menstrual cycles in 21 women with premenstrual exacerbations were studied and analysis of the group showed the peak flow to be significantly

Table 2 Peak flow measurements in 12 women without premenstrual exacerbations of asthma (34 menstrual cycles)

Week	Mean (SD) peak flow ($l\ min^{-1}$)	
	Morning	Evening
Premenstrual	335 (108)	347 (96)
Mid cycle	332 (115)	348 (105)
<i>t</i>	0.367	0.205
Significance	NS	NS

NS—not significant.

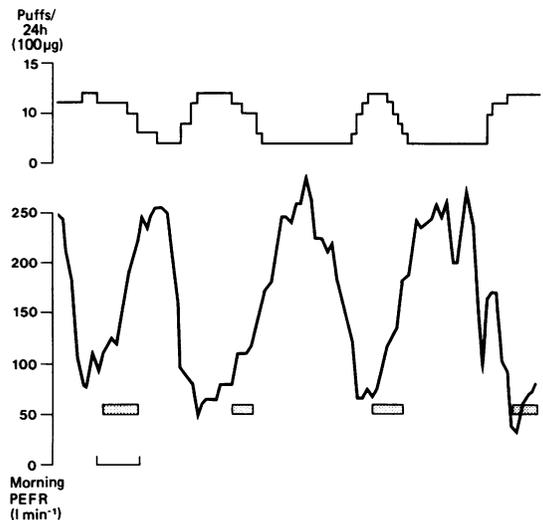


Fig 1 Peak flow (PEFR) recordings and use of salbutamol for one patient during three months in relation to menstruation (shaded areas). The scale below indicates one week.

lower in the premenstrual than the mid cycle week (table 1). There was no significant change in peak flow during the cycle in the 12 women who did not

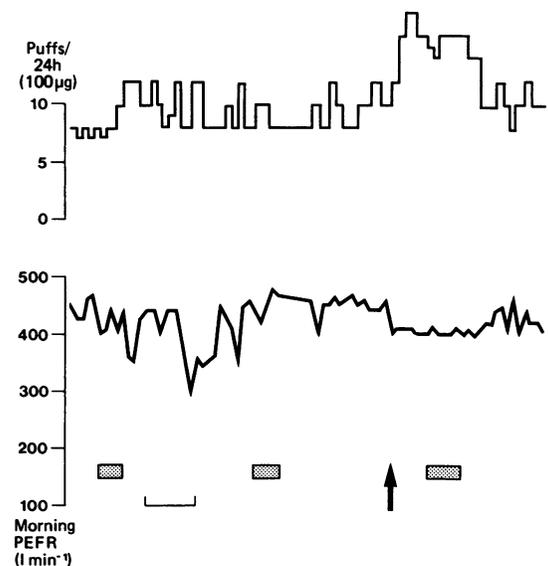


Fig 2 Peak flow (PEFR) recordings and use of salbutamol for another patient during three months in relation to menstruation (shaded areas). Her symptoms were particularly severe in relation to the third period as shown by the arrow.

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complain of premenstrual asthma (table 2).

Three of the patients complaining of premenstrual asthma had severe airways narrowing before every period and in one patient admission to hospital was frequently necessary (fig 1). These were the only patients in whom peak flow fell by more than 100 l min⁻¹.

Figure 2 shows the peak flow recordings of a patient whose symptoms of asthma were particularly severe during the premenstrual week of one cycle (marked by the arrow), resulting in a considerable increase in bronchodilator treatment. Yet at other times of the cycle similar or greater changes in peak flow did not result in the same awareness of symptoms or increase in treatment.

Discussion

Forty per cent of the women in this study reported premenstrual deterioration in their asthma and this was confirmed by serial peak flow measurements. Appreciable deterioration in peak flow before menstruation was, however, infrequent. The falls were usually modest and of a degree that would not be expected to result in increased breathlessness. Possibly there is not only a decrease in airway calibre before menstruation but also a heightened awareness of symptoms. The case illustrated in figure 2 provides some evidence for this. The fall in peak flow indicated by the arrow was associated with appreciable symptomatic deterioration requiring increased use of salbutamol, but similar falls at other times in the cycle were not associated with symptomatic deterioration or increase in treatment.

Premenstrual changes in mood and behaviour are known to occur¹ but we found no evidence that women with premenstrual worsening had more premenstrual tension, irritability, or depression than those whose asthma did not deteriorate. A previous study³ did find a higher incidence of premenstrual tension in patients with premenstrual asthma, but our assessment of premenstrual tension differed in that we did not include symptoms such as nausea and insomnia, which could be caused by either asthma itself or its treatment.

Impaired motor performance has been demonstrated in the premenstrual phase⁴ but we consider it unlikely that reduced ability to perform a simple expiratory flow manoeuvre could account for our results. Aspirin is well known to cause asthma in susceptible individuals and is commonly taken for premenstrual tension, but we found no relationship between aspirin consumption and premenstrual deterioration in asthma.

A previous study found that women whose asthma deteriorated at the time of the menstrual

period had a shorter cycle length,² but we were unable to confirm this observation. No consistent relationship emerged between use of the oral contraceptive pill and premenstrual deterioration.

The mechanism of the increased airflow obstruction occurring before menstruation is unknown. In the first description of the premenstrual tension syndrome Frank⁵ described a patient with premenstrual asthma who was treated by irradiation of the ovaries. She remained free of asthma for two and a half years. During this time she was amenorrhoeic, but her asthma recurred shortly before she resumed menstruation. Beaumont⁶ described a case of "ovarian asthma" which responded to progesterone treatment during the second half of the menstrual cycle and Dalton⁴ claimed success in treating premenstrual symptoms, including asthma, with progesterone pessaries. There has, however, been no controlled trial of progesterone in the treatment of premenstrual asthma. The serum progesterone concentration normally reaches a peak about seven days before menstruation and then rapidly falls almost to zero at the onset of the period.⁷ Since it is known that progesterone is a smooth muscle relaxant in the gut, genitourinary tract, and vascular tree,⁸ the fall in progesterone concentration in the late luteal phase might be associated with the withdrawal of a relaxant effect on bronchial smooth muscle.

Progesterone is known to cause hyperventilation^{9,10} and this might be perceived as increased dyspnoea, but the peak serum concentrations of progesterone are reached several days before symptomatic deterioration. This makes progesterone induced hyperventilation an unlikely explanation of our findings. We cannot, however, rule out the possibility that this mechanism may be operating in some cases where deterioration in peak flow began in mid cycle (fig 2).

Further studies to explain this phenomenon should examine possible changes in bronchial reactivity during the menstrual cycle and their relationships to hormone concentrations.

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