Aqueous humour turnover and intraocular pressure during menstruation

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SUMMARY Both intraocular pressure and aqueous humour turnover rate were determined at intervals over three months in three females in order to investigate whether a correlation existed between these variables and the menstrual cycle. Not only was there a lack of correlation between intraocular pressure or aqueous humour flow rate and menses but intraocular pressure and aqueous humour flow rate were also not related to each other. If pharmacologically administered doses of progesterone or oestrogen influence intraocular pressure, the present data indicate that the effect is probably mediated through effects on the aqueous outflow pathways.

The cyclical changes in oestrogeins and progesterones during the menstrual cycle are well documented.1,2 Despite several attempts, however, correlations between intraocular pressure (IOP), outflow facility (C), and the menstrual cycle have not been definitely proved.3 An increased IOP has been reported to occur immediately before, or during menstruation,4,5 while an increased C during the progestational phase and a decreased C during the oestrogenic phase has also been reported.6 Paterson and Miller,7 however, found a bicyclic increase in C which occurred in both the mid-oestrogenic and the mid-progesteronic phases. An increased occurrence of glaucoma symptoms, especially in angle-closure versus open-angle glaucoma patients, has also been noted during the menses.8 Although pharmacological doses of progesterone9,10 and oestrogen11,12 have been shown to induce small decreases in IOP, it is not clear whether naturally produced progesterone plays a role in IOP regulation.13

We have measured IOP and aqueous humour turnover rate with fluorimetry at weekly intervals in three female volunteers through at least three consecutive menstrual cycles in order to determine whether correlations exist between these parameters and the menstrual cycle.

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Materials and methods

Three normal female volunteers, free from eye and systemic disease, aged 27, 31, and 35, and not taking oral contraceptives, were recruited from the nursing and administrative staff of the Princess Alexandra Eye Pavilion. After signed, informed consent had been obtained a schedule was arranged to permit weekly determinations of fluorescein decay kinetics in the eye and IOP.

Each volunteer was given a calendar on which to mark the dates of menstruation and the date upon which they were tested. On the test day fluorocine eye drops (Fluress, Barnes-Hind, California) were either self administered or administered by a friend at a rate of one drop every two minutes between 0800 and 0830 h. Readings were taken of corneal and mid anterior chamber fluorescein (over the pupil) every hour for 4 or 5 hours beginning at 1300 h. Normal activities continued between readings. Fluorescein was detected by a Gamma scientific apparatus attached to a Haag-Streit 900 slit-lamp.14 Aqueous humour flow rate was determined according to the method of Jones and Maurice,15 using the linear decay of corneal and anterior chamber fluorescein after the peak concentrations had been reached.16 IOP was taken with a Goldmann tonometer immediately preceding the 1500 h reading. Determinations were made on as close to a weekly schedule as was possible. Unfortunately, over the last week of
Table 1  Aqueous humour fluorescein decay kinetics for subject 1

<table>
<thead>
<tr>
<th>Date</th>
<th>Eye</th>
<th>IOP (mmHg)</th>
<th>Slope (min⁻¹)</th>
<th>Flow (µl min⁻¹)</th>
<th>Kₘₐₓ (min⁻¹)</th>
<th>Menses</th>
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<tbody>
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<td>10 Feb to</td>
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For explanation of slope, flow, and Kₘₐₓ, see text.

1982 and the first week of 1983 it was impossible to schedule sessions.

Data analysis was performed only after the completion of the four-month study during which measurements were made without knowledge of the times of the menstrual cycle of the volunteers. The slope is the rate of decay of fluorescein in the anterior chamber expressed as the natural log of fluorescein concentrations. It has the dimension of min⁻¹, and was obtained by linear least squares methods. Kₘₐₓ is the transfer coefficient for fluorescein across the endothelium and has the dimension of min⁻¹. In order to calculate flow rate in µl min⁻¹ we assumed an anterior chamber value of 200 µl. Corneal volume was taken as 80 µl. While these values are slight overestimates of previously used values, they do reflect recent estimates of anterior chamber and corneal volumes.

Table 2  Aqueous humour fluorescein decay kinetics for subject 2

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<tr>
<th>Date</th>
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For explanation of slope, flow, and Kₘₐₓ, see text.
Table 3  Aqueous humour fluorescein decay kinetics for subject 3

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For explanation of slope, flow, and Kₓₓ, see text.

Results

The data obtained in this study are shown in Tables 1 to 3. While variations exist in all parameters as a function of time, none of the variations appear to be correlated with any part of the menstrual cycle.

IOP variations for the subjects varied between 10 and 16 mmHg, and, although the values differed at various times of the cycle, they did not correlate with it over the course of several cycles. The mean IOP and aqueous humour flow rate values for both eyes of each subject are shown in Figs. 1 and 2 respectively. These graphs illustrate the lack of correlation between these values and the occurrence of the menses.

Subject 1 tended to show a reduced IOP at or before the menstrual period for two of the four cycles, but her IOP was increased at other menses (Fig. 1). Subject 2 tended to have a slightly lower IOP after menses, although an exception occurred with the second menses in the testing series. No pattern existed for subject 3, whose IOP could not be even vaguely correlated with menses (Fig. 1). Similarly, in Fig. 2 it is evident that no relationship exists between aqueous humour flow rate and the menstrual cycle.

Fig. 1  Plot of intraocular pressure versus time. Each set of symbols corresponds to the identification shown in the upper block where the menses are indicated for each subject.
Comparison of Figs. 1 and 2 also illustrates that IOP can vary independently of aqueous humour flow rate.

Discussion

Fluorophotometry has proved valuable in assessing not only drug effects on aqueous humour dynamics but also in determining the changes in aqueous flow rate in a variety of clinical conditions. The validity of the technique has therefore been well proved. In the present study we assumed that the subjects had the same anterior chamber and corneal volumes, and, while this is probably not true, we were comparing changes which occurred with time in the same subjects, thus making the absolute value of the volumes of little importance. Nevertheless, the average values obtained for the slope, K, and aqueous flow rate are very similar to those published in other studies. Although the final number of subjects in the current study is small, the subjects were followed up for over three months, thus providing a longitudinal study of considerable duration, which is perhaps of more value than a shorter term study with more subjects. The subject drop-out rate was over 50% for several reasons.

Several studies have indicated an association between IOP or C and the menstrual cycle, although a variety of changes have been noted in relation to the phases of the menstrual cycle. Certainly the administration of pharmacological doses of progesterones and oestrogens (alone or in combination) has been recorded to induce a small fall in intraocular pressure in both experimental animals and man despite some findings to the contrary. The present study indicates that the assumed normal, physiological hormonal changes associated with the menstrual cycle in our subjects had no influence on either IOP or aqueous flow, confirming at least one earlier study. If progesterone or oestrogen has an effect at pharmacological dose levels the mode of action cannot be deduced from our studies, though the lack of effect on aqueous inflow in our study would suggest that the steroid effect would be directed primarily towards the outflow pathways. Evidence exists that outflow facility is affected both in normal females and in those subjects treated with progesterone-oestrogens as well as in experimental animals.

We thank our volunteers (B.S., R.G., and L.T.) for generously giving their time to permit this study, Mrs Sylvia Catravas for her excellent secretarial assistance, and R. David Elijah for performing the fluorescin computations. The Gamma scientific fluorophotometer was purchased with funds made available by National Glaucoma Research, a programme of the American Health Assistance Foundation. One of us (KG) was supported in part by a Fogarty Senior International Fellowship, FO6 TW00687, from the Fogarty Center, National Institutes of Health, Bethesda, Maryland.

We are grateful for the financial support of the W. H. Ross Foundation for the Study of the Prevention of Blindness.

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