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Hormonal Changes Associated with Menstrual Cycle Have No Definite Influence on Ocular Pressure

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ABSTRACT

Background: Despite some findings to the contrary, it would appear that pharmacological doses of progesterone and estrogen (alone or in combination) can influence intraocular pressure (IOP). The relationship between hormonal changes associated with the menstrual cycle and intraocular pressure is not clearly understood. After elimination of those factors that can affect IOP, the present study investigated whether physiological hormonal changes associated with the menstrual cycle have a correlation with intraocular pressure.

Methods: Intraocular pressure and the concentrations of circulating hormones, namely, the luteinizing hormone (LH), follicle-stimulating hormone (FSH), estrone (E1), estradiol (E2), progesterone, and testosterone, of twenty married women of the same age groups were recorded daily throughout a menstrual cycle. None was taking any contraceptives in any form. The intraocular pressure was measured using a Goldmann applanation tonometer.

Results: The intraocular pressure values fluctuated in each of the twenty subjects at various times of the cycle; however, they were not definitely correlated with the different phases of the cycle. This study failed to find any correlation between IOP and progesterone or estradiol levels.

Key Words: menstrual cycle; ocular tension; sex hormone; tonometry.

I. Introduction

Regarding the relationship between the days of the menstrual cycle and variations in intraocular pressure (IOP), findings have not been consistent. Elevated intraocular pressure just prior to or during menstruation has been reported by several observers (Paterson and Millar, 1963; Dalton, 1967; Bankes *et al.*, 1968). However, three studies have failed to find any relation between intraocular pressure and the days of the menstrual cycle (Feldman *et al.*, 1978; Green *et al.*, 1984; Gharagozloo and Brubaker, 1991). The relation between the menstrual cycle and intraocular pressure has been studied occasionally in the past but seldom recently. In recent years it has been noted that intraocular pressure is a dynamic function, subject to many influences both acutely and over the long term. Many investigators have reported that IOP varies with age (Qureshi, 1995) and diurnally (Xi *et al.*, 1996). It has been reported that drinking of water, coffee, or alcohol before measurement of IOP has a significant effect on it (Buckingham and Young, 1986). Several studies have also shown that intraocular pressure is positively correlated with systemic blood pressure (Klein and Klein, 1981). Moreover, acute hyperglycaemia decreases IOP (Poinoosawmy and Winder, 1984) while chronic hyperglycaemia in diabetes increases it (Williams *et al.*, 1980).

The existing literature shows that pharmacological doses of progesterone and estrogen (alone or in combination) can influence intraocular pressure (Becker and Friedenwald, 1953; Treister and Mannor,

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1970; Kass and Sears, 1977). The relationship between hormonal changes associated with the menstrual cycle and intraocular pressure is not clearly understood. Moreover, the inconsistent findings in previous studies may have been due to failure to control the above mentioned variables. Therefore, after taking control of these factors the present study investigated whether hormonal changes associated with the normal menstrual cycle have a correlation with intraocular pressure.

II. Subjects and Methods

All experimental procedures adhered to the Declaration of Helsinki of the World Medical Association. The work was approved by the Ethics Committee of the Institution and subjects gave informed consent to participate. Twenty married normal female volunteers, aged between 20 to 26 years, were recruited from working staff of the Eye and ENT Hospital, Shanghai Medical University-China. After their consent was obtained, a medical history was taken from each subject, including questions concerning previous ocular diseases, the presence of diabetes mellitus, and the occurrence of glaucoma in the family. The criteria met by the subjects were absence of ocular complaints including refractive errors; absence of any history of eye surgery and diabetes; normal body temperature and blood pressure; no contraceptives being taken in any form. In this study, only healthy subjects were included. Subjects were examined daily, including weekends and holidays, through a complete menstrual cycle.

Recently, we have reported (Xi *et al.*, 1996) that intraocular pressure varies diurnally, and that in the majority of subjects, IOP is highest in the morning. The subjects of this study were among those who had taken part in our previous study (Xi *et al.*, 1996), and all had the highest IOP in the morning. The subjects were examined at a fixed time between 09:00 and 10:00 hours to minimize the effect of diurnal variations. They were asked not to eat or drink tea and to rest for least 30 minutes before IOP measurement. The examination of the eyes included measurement of visual acuity using Snellen letters, tonometry, and ophthalmoscopy. After installation of 0.25% fluorescein sodium and 0.4% benoxinate hydrochloride (fluress) eye drops, IOP was measured using a Goldmann applanation tonometer (Goldmann Topcon, Germany), first in the right eye and then in the left, as has been described previously in detail (Qureshi, 1996). To avoid inter examiner variance, all the intraocular pressure measurements were taken by the same ophthalmologist and on a single tonometer. Three consecutive readings of each eye were taken. After each reading, the tonometer was removed from the contact, and the measuring scale was returned to 10 mmHg. The practice of returning the tonometer to 10 mmHg after each reading minimized observer bias. Immediately following IOP measurement, blood was drawn by veinpuncture and stored at -20 °C for subsequent radioimmunoassay to determine the blood concentrations of the circulating hormones, namely, the luteinizing hormone (LH), follicle-stimulating hormone (FSH), estrone (E1), estradiol (E2), progesterone, and testosterone. All of these hormones were measured according to the methods and instructions of the World Health Organization for the immunoassay of hormones (Sufi *et al.*, 1985)

Statistical Analyses: The mean of the three IOP readings was computed separately for each eye. For all the variables, descriptive statistics (mean, standard deviation, standard error of mean) were calculated using Statistical Analysis System 76 (Barr *et al.*, 1976). Analysis of variance (ANOVA) was used to compare the results of various days of the menstrual cycle. A separate analysis was performed to determine if a correlation existed between intraocular pressure and the serum progesterone level or between intraocular pressure and the serum estradiol level. A p value of less than 0.05 indicated that the correlation was significantly different from zero.

III. Results

From the data obtained by means of radioimmunoassay, the actual day of ovulation was determined for each woman by finding the day on which the blood level of LH was highest. This day of ovulation was then designated as the midpoint of the menstrual cycle, which we called day zero. The days prior to ovulation were referred to as "minus" days, and the days following ovulation as "plus" days. The results obtained by averaging the daily data obtained for each of the twenty women are shown in Fig. 1, which shows the curves for the values of the serum levels of Lh, FSH, E2 and progesterone. The level of testosterone was found to be almost constant throughout the cycle (data not shown) and the level of E1 almost parallel to that of E2. The results of averaging the daily IOP obtained for each of the twenty women are shown in Table 1. No significant difference was found between different days. The individual IOP data of three women are shown in Fig. 2. Although the IOP values differed in each subject on various days of the cycle, they did not correlate with each other. In subject 3, the highest IOP was found on the 7th day of the cycle while in subject 1, the lowest IOP was on this day

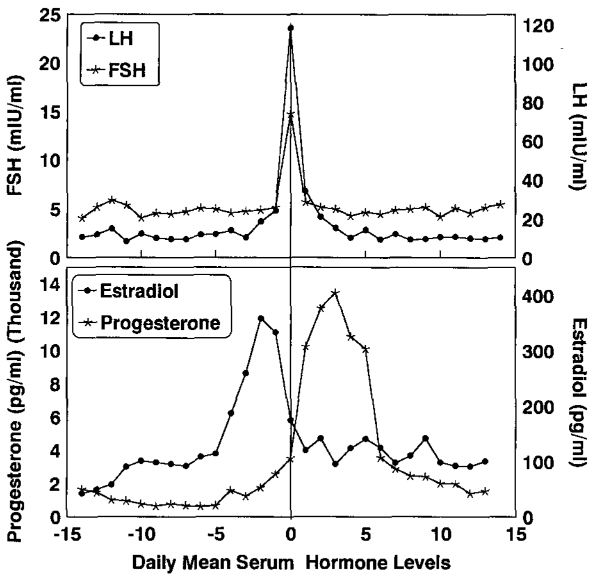

Fig. 1. Mean values of serum levels of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) above, and estradiol and progesterone below, throughout one menstrual cycle in twenty normal women. Each symbol corresponds to the identification shown in the round frame. (Standard deviations were less than 15 per cent of the mean values).

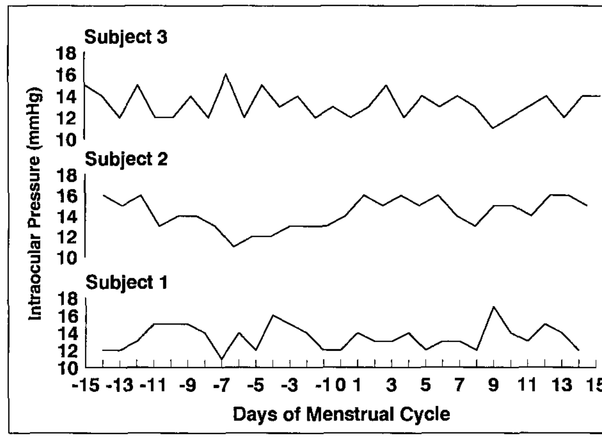

Fig. 2. Plot of intraocular pressure of three normal women versus days of the menstrual cycle. Variations in intraocular pressure existed in all the subjects, but these variations did not correlate with various days of the menstrual cycle.

of the cycle. Similarly, in subject 1, the highest IOP was found on the 9th day of the cycle while on the same day, the IOP in subject 3 was the lowest. On the other hand, in subject 2, there were many peaks and troughs. The IOP data of the 17 other women were similar and, thus, are not shown. The IOP fluctuations were similar in both eyes; therefore, only data of the right eye are shown. Table 1 shows the coefficients for the correlation between the serum progesterone level and IOP and between the serum estradiol level and IOP. The mean coefficients for the correlations of serum progesterone and estradiol levels with IOP of all the subjects were (meas ± SD) 0.11 ± 0.39 and 0.20 ± 0.61, respectively. These were not significantly different from zero.

IV. Discussion

Before the present study was carried out, only one study had measured intraocular pressure and sex hormones daily throughout the menstrual cycle (Feldman *et al.*, 1978). The present study has reported IOP changes throughout the menstrual cycle but failed to find any correlation between the variations of IOP and the days of the menstrual cycle. This result is in agreement with those of two other studies (Feldman *et al.*, 1978; Green *et al.*, 1984). Not only was the number of subjects in the current study higher than that in two previous studies (Feldman *et al.*, 1978; Green *et al.*, 1984), but we were also very fortunate in our choice of volunteers, for not one appointment was missed. Moreover, the present study tried to control all the factors that can effect IOP.

In the Bedford glaucoma survey, Bankes *et al.* (1968) found that the lowest mean IOP coincided with the 21st to the 24th days while the highest occur from the 9th through the 12th days, with another peak from the 25th through the 28th days of the menstrual cycle. Dalton (1967) also noted an increased incidence of glaucoma symptoms and elevated intraocular pressure in female glaucoma patients just before and during menstruation. In contrast to the results of these studies, those of the present study failed to find any definite effect of hormonal changes associated with menstrual cycle on IOP. This difference between

Table 1. Average of the Three Days IOP for Twenty Women and Coefficients for the Correlations between Progesterone and IOP, and between Estradiol and IOP

Days of cycle	IOP* (mmHg)	Correlation coefficients: Progesterone and IOP	Estradiol and IOP
1-3	14.7±1.8	0.91	0.63
4-6	14.1±2.1	0.00	-0.45
7-9	14.9±2.3	-0.63	0.82
10-12	14.2±2.8	-0.20	0.15
13-15	14.4±2.5	0.40	-0.17
16-18	14.4±1.7	1.00	0.46
19-21	15.1±2.9	-0.53	0.81
21-24	14.8±2.4	-0.40	-0.44
25-28	14.3±2.7	0.80	-0.25
29-30#	13.9±2.4	-0.22	0.56

*All values are mean ± SD. Difference between different days was found to be statistically insignificant.
#Only two women had a cycle of more than 28 days.

the present study and previous studies may be due to the fact that those investigators did not control diurnal variations or fluid intake, nor did they consider the blood pressure and diabetic status of their subjects. The mean coefficient for the correlation between the serum progesterone level and IOP, reported in this paper, is the same as that reported by Gharagozloo and Brubaker (1991). To the best of our knowledge, before the present study, the coefficient for the correlation between the serum estradiol level and IOP had never been studied.

Cyclic changes in estrogens and progesterones during the menstrual cycle are well documented (Feldman *et al.*, 1978; Green *et al.*, 1984; Guyton, 1991). Many investigators have noted variations in the aqueous fluid outflow facility over the course of a month in females (Becker and Friedenwald, 1953; Feldman *et al.*, 1978; Green *et al.*, 1984; Paterson and Millar, 1963), but in males these variations were absent (Kass and Sears, 1977). Several investigators have tried to find a correlation between the outflow facility and the levels of hormones during the cycle; however, their findings were not consistent and even contradicted each other. Becker and Friedenwald (1953) noted a relatively increased facility of aqueous outflow during the progestational phases and a decreased facility during the estrogenic phases of the menstrual cycle. On the contrary, Paterson and Miller (1963) noted an increased facility of outflow during the estrogenic and estrogenic progesterone phases of the menstrual cycle.

Although, several studies reported that pharmacological doses of progesterone and estrogen had effects on IOP values, their results were not consistent and even contradictory (Treister and Mannor, 1970; Kass and Sears, 1977). The data of this study indicate that hormonal changes associated with the menstrual cycle had no definite influence on intraocular pressure. The IOP measurements taken during the menstrual cycles in twins have not been described. Recently, it has been suggested that hereditary factors may play a role in the level of IOP (Kalenak and Paydar, 1995). The effect of physiological hormonal changes associated with the menstrual cycle on IOP can be better studied in twins. Therefore, we suggest a similar study in twin sisters and over the course of at least two menstrual cycles. ,

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IOP and Hormonal Changes During Menstrual Cycle

月經周期激素變化對眼內壓無明確影響

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摘　要

背景：目前認爲孕激素和雌激素（單獨或聯合）用葯可以影響到眼內壓 (IOP)，雖然有一些文獻持否定態度。隨月經周期而變化的激素與IOP之間的關係目前尚不明瞭。除去了可干擾IOP的影響因素後，本實驗試圖瞭解生理性隨月經周期而變化的激素是否引起IOP的改變。

方法：20個已婚同一年齡組且不用避孕葯的婦女在一個月經周期中，每日用Goldmann壓平眼壓計檢測IOP，並測定激素血液度，包括：黃體生成素 (LH) 、卵泡刺激素 (FSH) 、雌酮 (E1) 、雌二醇 (E2) 、孕激素和睪酮。

結果：20個對象的IOP值隨月經周期不同的時間而變化，然而未發現不同時期各激素水平與IOP間的確切關係。

結論：隨月經周期發生的激素改變對IOP無明確的影響。