Contact Lens & Anterior Eye 37 (2014) 209–212

Contents lists available at ScienceDirect

Contact Lens & Anterior Eye

journal homepage: www.elsevier.com/locate/clae

Changes in tear film, corneal topography, and refractive status in premenopausal women during menstrual cycle

Ercument Cavdar[a], Abdullah Ozkaya[b], Zeynep Alkin[b,*], Hande Mefkure Ozkaya[c], Mustafa Alparslan Babayigit[d]

[a] Kemalpasa State Hospital, Izmir, Turkey
[b] Beyoglu Eye Training and Research Hospital, Istanbul, Turkey
[c] Sisli Etfal Training and Research Hospital, Istanbul, Turkey
[d] Gulhane Military Medical Academy, Department of Public Health, Ankara, Turkey

ARTICLE INFO

Article history:
Received 25 July 2013
Received in revised form 5 November 2013
Accepted 20 November 2013

Keywords:
Tear film
Corneal topography
Refractive status
Menstrual cycle

ABSTRACT

Purpose: To investigate the changes in a questionnaire based subjective symptomatology, tear film break-up time, tear volume, corneal topography, and refractive status in premenopausal women during menstrual cycle.
Methods: Seventeen premenopausal females and 15 healthy males were enrolled in this prospective study. After routine ophthalmologic examination, an ocular surface disease index questionnaire was administered, tear film break-up time (TBUT), and Schirmer I tests were performed. Keratometry readings and refractive status were also obtained. All examinations were repeated at day 21, day 12 and day 2.
Results: OSDI score in day 21 was significantly lower than that in day 12 ($p = 0.004$) and day 2 ($p = 0.01$) in the female patients; however, no significant change was found in the male subjects ($p > 0.05$). No statistically significant difference was found in TBUT and Schirmer I tests, keratometry, and refraction results in both of the female and male subjects at all of the test points ($p > 0.05$). There was a significant correlation between OSDI score and TBUT ($p = 0.02$, $p = 0.03$, respectively), and Schirmer I test at day 12 ($p = 0.004$, $p = 0.008$, respectively). A significant negative correlation was found between oestrogen level and horizontal keratometry values at day 21 ($r = -0.5$, $p = 0.03$; $r = -0.4$, $p = 0.04$, respectively) for the right and left eyes in the female subjects.
Conclusion: Our study confirms that fluctuations in the blood levels of oestrogen produce alterations in ocular surface equilibrium during the menstrual cycle and consequently affect the subjective dry eye symptoms in female patients. However, no ocular surface parameter changes were observed.

1. Introduction

Oestrogen and progesterone receptors have been demonstrated in various ocular surface structures like cornea, lacrimal gland, meibomian gland, and palpebral and bulbar conjunctivae [1]. The changes in tear film and corneal parameters including corneal curvature, and corneal thickness were attributed to hormonal influences during the menstrual cycle in previous studies [2–5]. The two predominant hormones involved in the menstrual cycle are oestrogen and progesterone. The changes in oestrogen and progesterone throughout the menstrual cycle are well documented [2]. Plasma oestrogen levels increase in ovulation and in luteal phase during the menstrual cycle; however, plasma progesterone levels increase shortly before ovulation and rapidly decrease during luteal phase, until plasma oestrogen levels are paralleled. Oestrogen has been shown to diminish tear output produced by lacrimal gland and lipid secretion from sebaceous glands [6,7]. In addition, oestrogen can alter structural anatomy and physiological functions of the cornea by sodium reabsorption, water retention and ultimate tissue oedema [8].

To date, there is no study evaluating the changes in the ocular surface parameters and tear film during the menstrual cycle simultaneously, therefore this study was designed to understand these changes in healthy premenopausal women during menstrual cycle, either in the presence or absence of subjective symptoms of dry eye.

2. Methods

2.1. Subjects

This prospective, single-masked study included 34 eyes of 17 premenstrual females and 30 eyes of 15 healthy males. The nature

* Corresponding author at: Beyoglu Eye Training and Research Hospital, Bereketzade Cami Sok. No: 2, 34421 Beyoglu, Istanbul, Turkey. Tel.: +90 5052703658; fax: +90 2122526109.
E-mail address: zeynepalkin@gmail.com (Z. Alkin).

1367-0484/$ – see front matter
http://dx.doi.org/10.1016/j.clae.2013.11.005

of the study was described to all subjects who had volunteered to participate in the study. The subjects consented to take their part during the study period and inform the physician about the changes in ordinary status. This study was conducted in accordance with the Helsinki Decleration and local ethics committee approval was obtained.

The subjects who were using contact lenses or topical ophthalmic drugs, had a history of prior ocular surgery or trauma, or had ocular inflammatory or ocular surface disorders were excluded from the study. We also excluded the subjects who had any systemic disease or who were taking systemic medications and/or hormone replacement therapy during the 3-month period before the examination.

2.2. Procedures

All female subjects had regular menstrual cycles. The female subjects were asked to mark their calendars to keep a record of the cycle before the study and then measurements were started during a full menstrual cycle from the day 21. Considering the different cycle durations among the female subjects, we counted backward 21, 12, and 2 days before the first day of the next cycle for uniform data collection. The menstrual cycle was subdivided into follicular, ovulatory, and luteal phases. Day 21 represented the follicular phase, beginning with menstrual flow which is followed by increased level of oestrogen, day 12 represented the ovulatory phase, characterized by preovulatory oestrogen surge, and day 2 represented the luteal phase, in which increased levels of oestrogen and progesterone were detected. A gynaecologist documented oestrogen and progesterone concentrations with a finger prick blood test on the day of examinations to confirm that the female subjects were within an expected range for the intended phase of the cycle. All measurements were made with a single masked technique so that ophthalmologist had no knowledge of the stage of the menstrual cycle of the female subjects.

Slit-lamp biomicroscopy and fundoscopy were performed for each subject to confirm that there was no ophthalmologic pathology. Study parameters including OSDI questionnaire (ocular surface disease index), tear film break-up time (TBUT), Schirmer I test, manifest refraction with fogging technique, and keratometry (Nidek ARK-700A. Fremont, CA) were taken on day 21, day 12, and day 2 for each female subject. Ocular examinations and OSDI questionnaire were carried out in the male subjects at predetermined days in consistent with the menstrual cycle, which were as days 0, 10, and 19. For better understanding, these days were represented as day 21, day 12, and day 2. The repeatability of refractive error estimated by the Nidek autorefractor was shown in a study by Dobos et al. [9].

2.3. Ocular surface disease index questionnaire (OSDI)

The OSDI has been proven to represent sensitivity and specificity of normal subjects and dry eye patients [10]. Five levels of symptom were presented and these 5 levels of score ranged from 0 (none of the time) to 4 (all of the time). The OSDI overall score ranged from 0 which represents absence of a problem to 100 which represents the presence of worse symptoms. The total score of the questionnaire was calculated using the OSDI Formula. The 12-item questionnaires in OSDI include dry eye complaints and impact on the subject's life within the last week.

2.4. Tear film break-up time

Tear film break-up time (TBUT) is a test for the assessment of tear film stability. Commercially available fluorescein test paper was contacted to bottom conjunctiva and then removed. The subject was asked to blink three times and then look straight forward, without any blinking. The tear film is observed under cobalt-blue filtered light of the slit-lamp and the interval between the last blink and the first appearance of a dry spot or disruption in the tear film was measured. The procedure was repeated three times and the mean value was recorded. If TBUT value was below 10 s, it was accepted as abnormal.

2.5. Schirmer I test

The Schirmer I test was evaluated at least 5 min after the TBUT and performed under ambient light. After topical anaesthesia, a 35 mm × 5 mm size paper strip is placed at the junction of the middle and lateral thirds of the lower eye lid. The subject was instructed to look forward and to blink normally during the test. The length of the strip that was wet after 5 min was measured and accepted as the test result. A reading of less than 10 mm was considered abnormal.

2.6. Statistical analysis

A descriptive analysis was used for mean values during analysis. Friedman non-parametric test was performed to compare more than two dependent variables. Wilcoxon signed rank test was used for post hoc comparisons. In addition, multivariate regression analysis was performed to investigate the relationship between variables. Correlations between the variables performed on the same day of menstruel cycle were obtained. Statistical analysis was carried out with SPSS software (SPSS v 17.0; Inc., Chicago, IL). Significance level was set at $p < 0.05$ with 95% confidence interval.

3. Results

The study group consisted of 34 eyes of 17 premenopausal healthy females and control group consisted of 30 eyes of 15 healthy males. The mean age was 32.1 ± 7.2 years in the female subjects and 28.9 ± 4.8 years in the male subjects ($p = 0.16$). The mean duration of cycle in the female subjects was 26.1 ± 2.0 days.

A statistically significant difference in plasma oestrogen and progesterone levels was found between day 21 (follicular phase) and day 12 (ovulatory phase) ($p < 0.001$ for oestrogen, $p = 0.001$ for progesterone), between day 21 and day 2 (luteal phase) ($p < 0.0001$ for both), and between day 12 and day 2 ($p = 0.03$ for oestrogen, $p < 0.001$ for progesterone) which was convenient to the relevant phase of the menstrual cycle. Oestrogen and progesterone levels of the female subjects in day 21, 12, and 2 are listed in Table 1.

In the female subjects, OSDI score in day 21 was significantly lower than that in day 12 ($p = 0.004$), and day 2 ($p = 0.01$). However, no statistically significant difference was found between day 12 and day 2 ($p = 0.18$). In the male subjects, there was no statistically significant change in OSDI score during the study ($p > 0.05$ for all time points). The changes in TBUT, Schirmer I test in both of the female and male subjects were not statistically significant at all of the time points ($p > 0.05$ for all time points). OSDI score, TBUT, and Schirmer I test measurements of the subjects during the study are summarized in Tables 2 and 3.

In the female subjects, the results of linear regression analysis showed that OSDI score has a significant correlation with Schirmer I test in day 12 ($p = 0.004$ for the right eye, and $p = 0.008$ for the left eye, respectively), as well as with TBUT ($p = 0.02$ for the right eye, $p = 0.03$ for the left eye, respectively). Meanwhile, no significant correlation was found between OSDI score and the other variables in the male subjects at all of the time points ($p > 0.05$ for all time points).

As listed in Tables 4 and 5, vertical and horizontal keratometry measurements, spheric and sylindiric manifest refraction values