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Research Article

Variations in Intraocular Pressure During Different Phases of Menstrual Cycle

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Abstract

Aim: To evaluate Intraocular Pressure (IOP) variations during different phases of Menstrual cycle.

Methods: In this prospective study 100 emmetropic female subjects aged between 18 to 25 years were included to understand IOP changes through different menstrual phase. After a detailed ophthalmic examination non-eligible subjects were excluded from this study.

Results: ANOVA test shows the mean IOP for menstrual phase, proliferative phase and secretory phase in right eye was 13.851 mm Hg, 15.549 mm Hg, 15.961 mm Hg and in left eye was 14.748 mm Hg, 15.692 mm Hg and 16.062 mm Hg respectively. Statistically significant IOP changes found during the different phases of Menstrual Cycle, degrees of freedom= (2, 297) considering significance level at 5%.

Conclusion: During routine eye examination this statistically significant IOP changes between both eye throughout various menstrual cycle stages need to consider.

Keywords: Intraocular Pressure (IOP); Schiotz Tonometer; Menstrual phase; Proliferative phase; Secretory phase

1. Introduction

IOP refers to the pressure exerted by intraocular fluid in the eyeball. The normal IOP varies between 10-20 mm of Hg (mean value is 15.5 ± 2.5 mm of Hg) [1-3]. Change in IOP level depend on aqueous humor formation and outflow. Elevated IOP can lead to special type of optic neuropathy which results into deepening of the physiological cup and along with that the damage of the retinal ganglion cells which clinically manifest as defects in specific types of scotomas as visual field defect which leads to irreversible blindness. [4,5] Menstrual cycle is a set of cyclic changes which makes pregnancy possible in female reproductive system. Although this entire cycle take place in 28 days of average duration, this duration varies among individuals.

It is affected by contraceptive pills, steroid, sex hormones: Oestrogen, Progesterone, Follicle stimulating hormone (FSH) and Leuteinising hormone (LH). These hormones also have protective role in ocular diseases in women. Menstrual cycle comprises of 3 phases: First 1-4 days called as Menstrual phase, during this period level of oestrogen and progesterone falls. Between 5-14 days, called as Proliferative Phase, production of oestrogen increased and between 15-28 days, called as Secretory Phase production of progesterone increased. Various stage of menses is not generally considered while measuring IOP and other ocular examination [6-10]. Menses is essential for oocytes production and uterus preparation for pregnancy [7]. 80% of females reported some common symptoms including pimples, breast pain, tiredness, irritation, and mood swings during one to two weeks prior to menstruation [11]. In 20-30% of women these common symptoms, known as premenstrual syndrome, interfere with normal life. In 3 to 8% females, these symptoms are severe [8]. In developing country menarche occurs usually at the age of 12 -15 years, but in some individuals in develop country it may start at 8 years of age [9,10,12,13,14]. Bleeding during menstruation usually lasts for two days to one week. For a young woman, the length between two menstruation cycle is 21 to 45 days and for adult it takes 21 to 35 days (average e 28 days) [15]. Tonometry is used by eye care professionals to measure IOP [16]. Usually, unit to measure IOP is millimeter of mercury (mmHg). Literature shows that exercise has an impact on IOP, either positively or negatively [17,18]. Throughout the night and day IOP varies with a diurnal variation between 3 to 6 mm of Hg. This variation may increase in glaucomatous eyes. During the nighttime, despite the slower production of aqueous humour IOP may increase [19, 20]. Becker & Frieden Wald et.al noted a relatively increased outflow facility and minimal levels of ovarian hormones during progestational phase of menstrual cycle and decreased outflow facility and peak value of estrogen during estrogenic postmenstrual period [2]. In a study Bankers et.al measured 1,459 women's IOP by using Goldmann applanation tonometer in sitting position

from beginning days of last menses and observed that the lowest mean IOP coincided with 21st to 24th days while highest occurred from 9th to 12th days with another peak from 25th to 28th days of menses [3]. Prajna P et al., in their study on 75 emmetropic females, aged between 18 – 25 years, with regular menses, found a significant increase in IOP in secretory menses phase. Exclusion criteria of this study included females with irregular menstrual cycle, use of oral contraceptive pills, histories of hypertension, diabetes mellitus and using medication for bleeding. Schiotz tonometer was used to meased IOP in the three phases of Menses at 10 to 12 am [21]. Stoupel et.al had done a study on 27 healthy volunteers to measure IOP by using Perkins applanation tonometer and found that independently of temperature change, the increase of the atmospheric pressure (ATM) to 2 Bar significantly decreased IOP but when ATM was increased (60 min), the IOP decrease remained stable (IOP values were within normal range) and were independent of blood pressure change or corneal thickness. Again, when temperature was increased keeping ATM constant, did not change IOP i.e. only temperature increases did not influence the IOP significantly. Thus, it was found that environmental factors have significant effect on IOP [22]. Imran Ahmed Qureshi and Ekhtiar Shiarkar in their study of 103 emmetropic healthy subjects of age between 21 and 30 years from either gender showed that the average IOP during winter months were higher compared to spring, summer, and autumn months. This concluded that seasonal change has an impact on variations in IOP [23].

Many studies by various researchers had reported the different kind of changes of IOP during menstrual cycle. This current study aims to evaluate Intraocular Pressure (IOP) variations during different phases of Menstrual cycle.

In case, if this study proves that significant IOP changes exists throughout various phases of menses than it can be useful to make a proper diagnosis and plan of management of IOP related ocular changes, while performing routine eye examination for a female.

2. Methods

The study started after obtaining ethical clearance from the Institutional Ethical Committee. 100 emmetropic female subjects, aged between 18 to 25 years included in this prospective cross-sectional study. Patients with any ocular disease or with history of any eye surgery, Glaucoma, patients with systemic diseases like Hypertension, Diabetes mellitus. Patients taking contraceptives and pregnant women were excluded from this study.

For all subjects in the first step, after taking the consent form, demographic data and a detailed history including medical history, history previous ocular diseases or surgeries and history medications use. Then all the subjects in this study had undergone ocular examination like distance visual acuity testing using Snellen chart at 6m and near visual acuity with the help of reduced Snellen's chart at 40cm, objective and subjective refraction, cover test, facial symmetry test, Hirschberg test followed by slit-lamp examination and fundoscopy. Schiotz Tonometer was

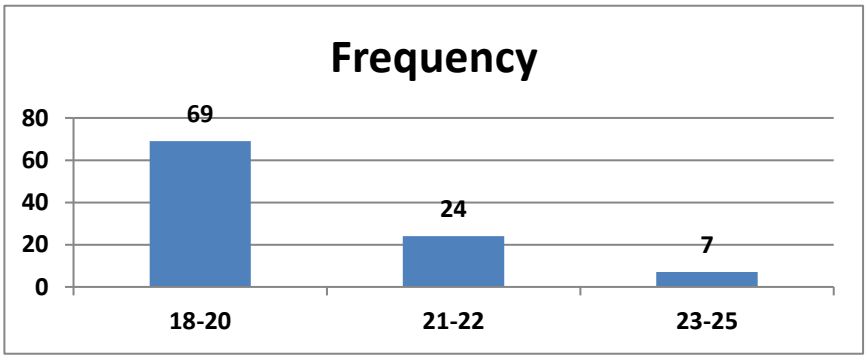
used to measure in all the 3 phases of Menses. Once between 1st to 5th day in Menstrual phase, second between 6th to 14th day in Proliferative phase and lastly between 15th to 28th day in secretory phase. All the procedure including measurement of IOP was taken at a fixed time from 9:00 – 10 am to minimize diurnal variations effect. The history of their menstruation date was also recorded so that, they can be called on their exact date of menstrual in the next month to take the measurement.

Statistical analysis was done with the help of ANOVA with Turkey HSD test through SPSS version 17.0. In this analysis P <0.05 implies that the data is showing statistically significant difference whereas P<0.01 implies highly significant difference and P<0.001 implies that the data is very highly significant difference.

3. Results

Mean age of 100 subjects enrolled in this study were 20.01 years.

3.1 Graph 1: Bar diagram showing the age wise distribution of total subjects.



Graph 1: Shows that, there were 69 subjects who fall age group between 18-20 years, 24 subjects in age group between 21-22 years and 7 subjects who were found in the age group between 23-25 years.

3.2 Table 1: Mean IOP values in right eye in different phases of menstrual cycle

Phases of Menstrual Cycle	Mean IOP value
Menstrual Phase	13.851
Proliferative Phase	15.549
Secretory Phase	15.961

Table 1: Shows mean IOP values of Right Eye in Menstrual phase were 13.851, in Proliferative phase were 15.549 and in Secretory phase were 15.961.

3.3 Table 2: Mean IOP values in left eye in different phases of menstrual cycle

Phases of menstrual cycle	**Mean IOP value**
Menstrual Phase	14.748
Proliferative Phase	15.692
Secretory Phase	16.062

Table 2: Shows mean IOP values of Left Eye in Menstrual phase were 13.851, in Proliferative phase were 15.692 and in Secretory phase were 16.062.

3.4 Table 3: Mean and standard deviation of IOP in right eye in different phases of menstrual cycle.

Phase	**N**	**Mean**	**Std. Deviation**	**F**	**P**
Menstrual Phase	100	13.851	3.729		
Proliferative phase	100	15.549	2.582		
Secretory phase	100	15.961	3.071	12.51	<0.001

Table 3: Shows mean IOP values of Right Eye in Menstrual phase were 13.851, in Proliferative phase were 15.549 and in Secretory phase were 15.961 and the standard deviation in Menstrual phase were 3.729, in Proliferative phase were 2.582 and in Secretory phase were 3.071 which indicated very highly significant difference in IOP throughout various phases of menses in Right Eye.

3.4 Table 4: Multiple comparisons of IOP in right eye between different phases of menstrual cycle.

Multiple Comparisons (Tukey HSD)				
Dependent Variable	(I) group	(J) group	Mean Difference (I-J)	Sig.
	Menstrual Phase	Proliferative phase	-1.698	<0.001
		Secretory phase	-2.11	<0.001
	Proliferative phase	Secretory phase	-0.412	0.627

Table 4: Shows that, there were very highly significant changes in IOP between Menstrual phase with Proliferative and Secretory phase and no significant changes between Proliferative phase with Secretory phase in Right Eye.

3.5 Table 5: Mean and standard deviation of IOP values in left eye in different phases of menstrual cycle

Phase	N	Mean	Std. Deviation	P
Menstrual Phase	100	14.748	3.316	
Proliferative phase	100	15.692	2.425	
Secretory phase	100	16.062	2.289	<0.001

Table 5: Shows mean IOP values of Left Eye in Menstrual phase were 14.748, in Proliferative phase were 15.692 and in Secretory phase were 16.062 and the standard deviation in Menstrual phase were 3.316, in Proliferative phase were 2.425 and in Secretory phase were 2.289 which shows a very highly significant changes in IOP throughout various phases of Menses in Left Eye.

3.6 Table 6: Multiple Comparisons of IOP in Left Eye between different phases of Menstrual Cycle.

Multiple Comparisons (Tukey HSD) of dependent Variable			
(I) group	(J) group	Mean Difference (I-J)	Sig.
Menstrual Phase	Proliferative phase	-0.94400	0.038
	Secretory phase	-1.31400	0.002
Proliferative phase	Secretory phase	-0.37000	0.600

Table 6: Shows that, there were significant difference in IOP between Menstrual phase and Proliferative phase, highly significant difference between Menstrual phase and Secretory phase and no significant difference between Proliferative phase and Secretory phase in Left Eye.

4.Discussion

The age group selected is 18-25 years non pregnant women group. In this study all subjects studied had 28 days cycle only.

Collagen fiber synthesis in female activates by oestrogen. Thus, the increased amount of collagen fiber at the lamina cribrosa, improve the structures compliance, which relieves compression on RBC axons aiding in their survival. Flexibility of whole eye can also enhance by increased collagen fiber resulting decreased IOP. Similarly, Oestrogen also stimulates pituitary secretion of thyroid, gonads, adrenals, and breasts. Increased secretion of oestrogen causes increased secretion of Antidiuretic Hormone and growth hormone which can cause increased IOP, raised blood pressure, weight gain, etc [24]. In our

study after statistical analysis, we found, IOP varies significantly throughout phases of menses which may be due to fluctuation of female sex hormones during these phases, the level being highest in menstrual phase but lowest during secretory phase.

Kiely et. al while studding changes in women's corneal curvature throughout menstrual cycle found that, for both horizontal as well as vertical meridian steepening occurs at follicular phase of menses due to decreasing of estrogen level and flattening occurs at luteal phase because of increasing in levels of female sex hormones. These changes are important for any female glaucoma patients during their eye evaluation and IOP measurement [2].

Bankers et.al, found the lowest mean IOP coincided with 16^{th} to 19^{th} days (13.3 ± 0.6) i.e., during their secretory phase while highest occurred from 20^{th} to 22^{nd} days (14.9 ± 0.2) i.e., during their secretory phase and another peak from 13^{th} to 15^{th} days (14.8 ± 0.3) i.e., during proliferative phase of menses in which IOP were measured by Goldmann applanation tonometer. But in our study, the lowest mean IOP occurred during menstrual phase (13.851 in right eye and 14.748 in left eye) and the highest mean IOP occurred during secretory phase (15.961 in right eye and 16.062 in left eye) of menstrual cycle in which IOP was measured by Schiotz tonometer [3].

According to Prajna P et. al. a significant increase of IOP in the secretory phase of menstrual cycle may be caused due to low levels of oestrogen and progesterone hormone during this phase [21]. Our study shows significant variations in IOP during different phases of Menstrual cycle. Multiple comparisons in IOP between three different phases of Menses in Right eye showed that, IOP variations between Menstrual phase with Proliferative and Secretory phase were very highly significant while between proliferative and secretory phase were not significant which can be caused by increased production of oestrogen during proliferative phase and progesterone during secretory phases of Menses. Similarly, multiple comparisons in IOP between three different phases of Menses in Left eye showed that, IOP variations between Menstrual and Proliferative phase were significant, between Menstrual and secretory phase were highly significant but between Proliferative and luteal phase were not significant which may be due to decreased production of progesterone during follicular phase and decreased production of oestrogen during luteal phase of Menstrual cycle.

In this study all subjects were selected from one particular region, variations in IOP due to changes in blood pressure or environmental factors was not considered and IOP was taken in a particular time in a day for each patient. Hormonal blood test was not done to check the variation in level of Hormones. These were few limitation factors for this current study.

Ocular conditions related to IOP can be diagnosed in a better way. IOP measurement, diurnal variations and its relationship with different stages of menses can be studied. Further, future studies can be done to understand the IOP changes during menses for different age groups and in patient with glaucoma. **In this study moreover no hormonal profile has been**

assessed to corelate directly the IOP changes to hormonal changes like oestrogen, progesterone, or LH. In future even this can be considered as a scope of study for researcher.

5. Conclusions

This study concluded throughout various phases of menses a statistically significant IOP changes present may be due to fluctuation of female sex hormones during this period. Hormonal level will certainly vary on varying days of the cycle, particularly if all the subjects were not having exactly 28 days cycle periods. With this it is difficult to positively conclude that too using limited sample size. During routine eye examination this statistically significant IOP changes between both eye throughout various menstrual cycle stages need to consider. The fluctuation of IOP can help to plan for intraocular surgeries.

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