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Research Article

Diurnal Variation of Intra Ocular Pressure (IOP) in Healthy Individuals: A Pilot Study

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Abstract: Aqueous flow has a distinctive circadian rhythm, being lower at night than during the day. IOP fluctuates in a rhythmical diurnal pattern and this fluctuation is greater in eyes with glaucoma.The total number of subjects included in the study was 100 apparently healthy individuals (non-glaucomatous and not suffering from any other ocular problem). Of these 100 individuals, 50 were men and 50 women in the age groups 20-40 and 41-60years. According to the results from our study , IOP in the morning when compared with the afternoon IOP showed a decrease of 3.1 mmHg (21.5 %) & 2.41 mmHg(17.97 %) in IOP in Right and left eye 's in Men of 20-40 years age group & a decrease of 2.27mmHg(12.03 %) & 2.29 mmHg (12.84 %) in IOP in Right and left eye's in women of 20-40 years age group. Similarly, IOP showed a decrease of 2.26 mmHg(14.47%) & 2.98 mmHg (20.58 %) in IOP in Right and left eye 's in Men of 40-60 years age group & a decrease of 2.07 mmHg(10.80 %) & 1.62 mmHg (8.95%) in Right and left eye's in women of 40-60 years age group was observed . In our study, we found a peak (maximum) IOP around morning and trough (minimum) IOP in the afternoon in majority of the subjects.
Keywords: Intraocular pressure; Diurnal variation; Glaucoma; Aqueous humour

INTRODUCTION:

Intraocular pressure is a function of aqueous humor drainage from the eye. Formed by the ciliary body located slightly behind and lateral to the lens, aqueous humor flows between the iris and lens, through the pupil into the anterior chamber, and drains out via the trabecular network and canal of Schlemm into the extra ocular veins at the rate of 2 to 3 µL/min. Resistance to free drainage is the primary mechanism maintaining aqueous humor volume and in normal individuals the mean IOP is 15.5 ± 2.5 mmHg. Aqueous flow has a distinctive circadian rhythm, being lower at night than during the day. Outflow facility in healthy human eyes is the range of 0.1 to 0.4 µL/min/mmHg. Episcleral venous pressure in healthy humans is 8 to 10 mmHg. Tonometry refers to the indirect estimation of intraocular pressure by measuring resistance of the eye to indentation by an applied force. The aqueous humor leaves the eye by passive flow via two pathways - the trabecular meshwork (TM) and the uveoscleral pathway. In humans, 75% of the resistance to aqueous humor outflow is localized within the TM with the juxtacanalicular portion of the TM being the main site of outflow resistance. Glycosaminoglycan deposition in the TM extracellular matrix (ECM) has been suggested to be responsible for increased outflow resistance at this specific site whereas others have suggested deposition of proteins, such as cochlin, obstruct the aqueous humor outflow through the TM. The uveoscleral outflow pathway is relatively independent of the intraocular pressure and the proportion of aqueous humor exiting the eye via the uveoscleral pathway decreases with age [1].

Intraocular pressure is not a constant value rather it varies based on a number of factors. The short-acting influences were food or fluid intake, variations in systemic blood pressure and excessive physical activity. The pattern of variation in the IOP over the course of 24 hours may be related to other diurnal endogenous variations in the body, such as the production of cortisol. There appears to be consistent seasonal variations in IOP. Such variations are of particular interest in glaucoma, where elevated IOP is assumed to be associated with damage to retinal nerve fibers leading to loss in the visual field and even blindness. IOP precisely follows circadian rhythm.

The variations in IOP may be due to simple mechanical factors. One such mechanical factor is the tension in the intraocular muscles and the effect they have as they compress the globe during contracture having accommodation, with corresponding contraction of the ciliary muscles. Armaly and Jepson [2] showed that accommodation can reduce IOP. During sleep there will be less accommodative effort than at other times. Another possible factor is alterations in blink pattern, particularly during sleep, which may have influence on the episcleral veins and the collector channel on the surface of the globe near the limbus. It has been shown that blinking raises the IOP instantaneously and a forceful hard blink may raise the IOP by as much as 50 mm Hg. Brubaker [3] recently suggested that the acute

rises in IOP following sleep reported by Brown and co-workers and by Zeimer & co-workers [4] might be due to an acute rise in systemic blood pressure that pumped an increased volume of blood into the eye.

Recent studies have suggested that intraocular pressure is regulated by the adrenal cortex. A relation has been demonstrated between maximal and minimal levels of diurnal tension measurements and plasma levels of 17-hydroxycorticosteroids. According to Roetth A Jr [5] osmotic changes in the blood might play a role in diurnal pressure variations through changes in aqueous inflow. However, diet, fasting, rest, or exercises do not alter the tension curve.

Barany [6] has proposed a mathematical formulation to show how the steady-state value of intraocular pressure depends on rate of secretion, episcleral venous pressure, outflow facility at the chamber angle, colloid osmotic pressure of the blood, systemic arterial blood pressure, pressure distribution over the vascular tree of the eye, and filtration properties of the vasculature in different intraocular regions. The daily maximum pressure in normal eyes is likely to be due to an increase in aqueous inflow and that of glaucomatous eyes by a decrease in outflow facility.

Like many other biological parameters, the IOP is subject to cyclic fluctuations throughout the day. The reported mean amplitude of the daily fluctuation ranges from approximately 3- 6mmHg. Amplitude greater than 10 mmHg is generally considered to be pathologic and glaucomatous eyes have been reported to exceed 30mmHg of diurnal variation. The pattern of the daily cycles has classically been described as having the peak IOP in the morning hours. IOP, Retinal function, Axial length, Pupil size, Palpebral tissue width and tonic accommodation exhibit diurnal variation. The IOP is maintained at its normal level by balance between the hydrostatic pressure in the capillaries and the difference between the osmotic pressure of the aqueous humor and the capillary plasma.

MATERIALS AND METHODS

The total subjects that are needed for the purpose of study are 100 apparently healthy individuals (non-glaucomatous and not suffering from any other ocular problem). Of these 100 individuals 50 were men and 50 women, with ages ranging between 20 and 60 years. The entire study was carried out at Dr.Pinnamaneni Siddhartha Institute of Medical Sciences and Research Foundation, Chinnaoutpalli. The subjects were chosen from the staff and students of Dr.Pinnamaneni Siddhartha Institute of Medical Sciences and Research Foundation, Chinnaoutpalli . In both the genders, there are two age groups viz., 20-40 and 41-60 years (in men there are two age groups and also in women, two age groups). Each age group holds up 25 individuals. For the present study the intraocular pressure values were taken from all the individuals using a Schiotz Tonometer (Improved). From each individual two measurements (first measurement in morning and second in afternoon) were taken on the same day. This is to study the difference between morning and afternoon values of intraocular pressure in every subject. The timing of the first reading was between 9:00 and 10:00 a.m and on the other hand second reading between 3:00 and 4:00 p.m. Informed consent was taken from the subjects. The study was approved by the Institutional Ethics Committee.

RESULTS

Statistical Analysis

Statistical analysis was done using Graph pad prism 6. Un-paired t test was used. p value < 0.05 was considered as significant.

In the Morning, in 20-40 years age group, the mean IOP in male subjects was 14.40 ± 0.2488 mmHg & 13.41 ± 0.2554 mm Hg in the Right and Left eye respectively & the mean IOP in female subjects was 18.86 ± 0.2421 mm Hg & 17.83 ± 0.2455 mm Hg in the Right and Left eye respectively. In the Afternoon, in 20-40 years age group, the mean IOP in male subjects was 11.73 ± 0.2779 mm Hg & 11.0 ± 0.2262 mm Hg in the Right and Left eye respectively & the mean IOP in female subjects was 16.59 ± 0.2549 mm Hg & 15.54± 0.2286 mm Hg in the Right and Left eye respectively .

In the Morning, in 40-60 years age group, the mean IOP in male subjects was 15.61 ± 0.2684 mm Hg & 14.48 ± 0.2333 mm Hg in the Right and Left eye respectively & the mean IOP in female subjects was 19.15 ± 0.1873 mm Hg & 18.1 ± 0.1945 mm Hg in the Right and Left eye respectively. In the Afternoon, in 40-60 years age group, the mean IOP in male subjects was 13.34 ± 0.3503 mm Hg & 11.5± 0.4638 mm Hg in the Right and Left eye respectively & the mean IOP in female subjects was 17.08 ± 0.1825 mm Hg & 16.48± 0.1795 mm Hg in the Right and Left eye respectively.

From the results of our study , we found that IOP in the morning when compared with the afternoon IOP showed a decrease of 3.1 mm Hg (21.5 %) & 2.41mm Hg (17.97%) in IOP in Right and left eye ‘s in Men of 20-40 years age group(p value <0.0001 in both right and left eye) & a decrease of 2.27 mm Hg (12.03%) & 2.29 mm Hg (12.84 %) in IOP in Right and left eye’s in women of 20-40 years age group (p value <0.0001 in both right and left eye). A decrease of 2.26 mm Hg (14.47%) & 2.98 mm Hg (20.58%) in IOP in Right and left eye‘s in Men of 40-60 years age group & a decrease of 2.07 mm Hg (10.80%) & 1.62 mmHg (8.95%) in Right and left eye’s in women of 40-60 years age group was observed, when IOP in the morning was compared with the afternoon IOP (p value <0.0001 in both right and left eye).

Table 1: Mean IOP value's in Male & Female subjects in 20-40 years age

	IOP(Morning) (20-40 Age Group)	IOP(Afternoon) 20-40 Age Group	P-Value
Male Right Eye	14.40 ± 0.2488	11.73 ± 0.2779	< 0.0001 ****
Male Left Eye	13.41 ± 0.2554	11.00 ± 0.2262	< 0.0001 ****
Female Right Eye	18.86 ± 0.2421	16.59 ± 0.2549	< 0.0001 ****
Female Left Eye	17.83 ± 0.2455	15.54 ± 0.2286	< 0.0001 ****

Table 2: Mean IOP value's in Male & Female subjects in 40-60 years age

	IOP(Morning) (40-60 Age Group)	IOP(Afternoon) (40-60 Age Group)	P-Value
Male Right Eye	15.61 ± 0.2684	13.34 ± 0.3503	< 0.0001 ****
Male Left Eye	14.48 ± 0.2333	11.50 ± 0.4638	< 0.0001 ****
Female Right Eye	19.15 ± 0.1873	17.08 ± 0.1825	< 0.0001****
Female Left Eye	18.10 ± 0.1945	16.48 ± 0.1795	< 0.0001 ****

DISCUSSION

Although the results from many studies on diurnal variation in intraocular pressure over a 24 hour period are conflicting, some of these differences in IOP can be attributed to the testing techniques; differences in tonometers; the frequency of IOP measurements and other factors like environment and posture. All these factors confer important contributions to the diurnal variation in IOP.

The different mechanisms which may cause the diurnal variation in IOP are: hormonal levels in the body like plasma cortisol; autonomic control of aqueous outflow from eye; variation in the production of aqueous humor; mechanical factors (like tension in the intraocular muscles; contraction of ciliary muscles; alterations in blink pattern); acute raise in systemic blood pressure.

Tielsch [7] found that the highest IOP occurred between 5 and 7 AM before the patients arose. Ericson [8] studied 50 female nursing students aged 20 to 28 years. Their IOP values were given as Schiotz readings rather than millimeters of mercury. The values were highest at 8 AM. Lowest value was during the day at 4 PM. Katavisto [9] studied 50 hospitalized individuals with normal IOP, half men and half women. The highest IOP values were detected at 8 AM (41% of the eyes). Over 20% of the subjects had their highest values at midnight. The diurnal variation averaged 3.17 mm Hg. Drance [10] studied 306 eyes of hospitalized individuals with normal IOP and found that 42% had their higher IOP at 6 AM; the mean diurnal range was 3.7 mm Hg.

Aachal Kotecha *et al.* [11] Heath examined the relationship between diurnal variations in IOP measurements, central corneal thickness and corneal hysteresis. IOP was measured with Goldmann applanation tonometer (GAT) and Dynamic contour tonometer (DCT). They observed that the central corneal thickness followed a diurnal pattern similar to the IOP, being thickest on awakening and reductions through the day. Goldmann applanation tonometer IOP measurements were greatest in the morning and reduced gradually during the day. They suggested that the peak in measured IOP often seen in early morning may be explained in part by the effects of a hydration related corneal thickness increase, induced by overnight eye closure. The results of our study were in accordance with this study. Jonathan S. Pointer [12] studied about the diurnal variation of IOP in Non-glaucomatous subjects. He observed that in readings between the hours at 9.00 and 18.00, human non-glaucomatous males and females registered an IOP peak in the late morning succeeded by a lowered value from mid-afternoon. The pattern of IOP change (i.e., a period of elevation above the mean in late morning and a depression around mid-afternoon) in this study is in agreement with the previous studies. Also, the results of our study were in accordance with this study. Klein BE; Klein R; Liston KL [13] conducted a population based study of age related eye diseases in persons 43-86 yr of age. They observed that the mean IOP increased significantly with age. Mean IOP differed little between sexes and was most significantly different after age adjustment. Also, they concluded that there was an association of IOP with systolic and diastolic blood pressures, body mass index, hematocrit, serum glucose, glycohemoglobin, cholesterol level, season and time of day of measurement (The Beaver Dam Eye Study).

Paul Henkind *et al.* [14] studied about the relation between ocular tension measurements with other physiologic and biochemical parameters in man. They observed that the IOP was lowest in the early morning generally around 3 a.m. which is at variance with most published data reporting lowest values of IOP during afternoon. Arthus J Sit *et al.* [15] investigated the circadian variation of aqueous dynamics in young healthy adults. They found that the 24 hr IOP pattern is due to circadian variations in episcleral venous pressure (EVP) or a combination of factors. They concluded that

EVP may be a critical parameter for the control of nocturnal IOP elevation.

John HK. Liu *et al.* [16] studied about the twenty four hour pattern of IOP in the aging population (50-69 yrs of age). They observed that the mean IOP in the dark period was significantly higher than mean IOP in the light/wake period. The main factors in the nocturnal IOP elevation may be due to shift from daytime upright posture to supine posture at night. Romanet JP *et al.* [17] measured the nyctohemeral variations in IOP (the full 24 hour period of a night and Day). They concluded that IOP follows a nyctohemeral rhythm and in healthy subjects, IOP was higher at night than during the day, with a nocturnal peak value. Sihota R *et al.* [18] worked to evaluate the circadian rhythm of IOP in Primary closed angle glaucoma , primary open angle glaucoma and in normal eyes. They observed that diurnal IOP fluctuations were significantly higher in primary closed angle chronic glaucoma(PCACG) (7.69 ± 3.03 mmHg) and primary open angle glaucoma (POAG) (8.31 ± 2.58 mmHg) groups compared to normal controls (4.83 ± 2.46 mmHg). They found that Afternoon peaks are more common in post iridotomy primary closed angle chronic glaucoma eyes & Morning peaks are more frequent in primary open angle glaucoma eyes. Yong Kyu Kim *et al.* [19] investigated about the circadian pattern of BP, IOP & mean ocular perfusion pressure (MOPP) while experiencing undisturbed sleep in normal tension glaucoma & non – glaucoma control patient groups. Normal tension glaucoma group showed a significantly large morning BP dip compared to control group. They observed that in both Groups, the mean IOP was low during Night time and high during day time, especially in the early morning. Tajunisah I *et al.* [20] conducted a case controlled prospective study to evaluate the diurnal variation of IOP; the mean, amplitude of variation and the peak & trough times of pressure readings in the suspected open angle glaucoma patients as compared with a control group. They observed that the highest percentage of control group had peak readings in the late evening (6-7 p.m.) and trough readings after midnight (2-3 a.m.) .The observations from our study varies with this study.

Boyd TAS *et al.* [21] reviewed about the relation of diurnal variation of plasma corticoid levels and IOP in glaucomatous and normal eye's. They observed that both maximum and minimum values of corticoids & IOP tend to be exactly in phase. They observed that the plasma corticoids were highest from 8.00 a.m. to 4.00 p.m. & lowest from 8.00 p.m to 4.00 a.m. The IOP values were highest from noon to 8.00 p.m. & lowest from midnight to 8.00 a.m.

Using fluorophotometry, diurnal variations were observed in aqueous humor turnover rates, reflecting a pattern known as the circadian rhythm of aqueous humor flow in humans. Aqueous humor flow is higher in the morning than at night. Aqueous humor flow is normally about 3.0µl/min in the morning, 2.4µl/min in the afternoon, and drops to 1.5µl/min at night [22].

CONCLUSION

A number of theories about mechanisms that modulate the diurnal fluctuations in IOP are related to the clinical findings. Those who found the highest IOP in the morning on awakening have concentrated on the mechanical factors relating to sleeping and lying down. Those who had found higher IOP at other times have tended to concentrate on hormonal or neural factors. The variation in IOP may be due to alteration in some of the normal homeostatic mechanisms in the eyes. The knowledge that there is a diurnal variation in IOP has a special application in glaucoma screening programme's. Also, the IOP peaks over a certain level or a diurnal range in IOP above a level might be diagnostic of glaucoma even in the absence of visual field loss or glaucomatous cupping. It was also accepted that diurnal IOP measurement plays an important role in the diagnosis of low tension glaucoma.

In our study, we found a peak (maximum) IOP around morning and trough (minimum) IOP in the afternoon in majority of the subjects. As we have taken only 2 readings: one in morning and another in the afternoon, these readings may not reflect the absolute changes in IOP.

In our study, we measured IOP using Schiotz tonometer (with the subject in supine position). The effect of posture on IOP was not taken into consideration. Even though the technicians were trained to use the Schiotz tonometer, user inexperience may be one of the sources of error. In regular practice, the significance of diurnal variation of intraocular pressure, age group, gender and posture should be taken into consideration. In many studies, the morning IOP has often been the time when relatively higher IOP values have been recorded, with the range of the diurnal variation being 3-5 mmHg. The outcome of the present study extends this result of being particular relevance to the screening and monitoring of subjects at risk of developing glaucoma. Data on the variation in IOP values are important for the diagnosis, treatment and prognosis of glaucoma. The peak IOP may be the parameter that best correlates with the prognosis of glaucoma.

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