

DIURNAL VARIATION IN THE CARDIOVASCULAR INDICES AND INTRAOCULAR PRESSURE

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Abstract

Introduction: Intra ocular pressure is an essential entity in maintaining the structural and functional integrity of eye ball. It varies in regular cycle in the normal eye for 24hour. In the present study, the diurnal variation of Heart rate, intra ocular pressure, systolic, diastolic, pulse and mean arterial pressures from 6AM to 6PM with every 2 hour interval was investigated.

Methodology: The present study included 100 normal male healthy subjects from the Gulbarga city, recruited after their informed and written consent. Intra ocular pressure, Heart rate, Blood pressure, Temperature, Urine output and respiratory rate per minute was investigated in all the subjects. Diurnal variation of Intra ocular pressure, Blood pressure, heart rate was measured at every 2hrs from 6 AM to 6 PM.

Result: The diurnal variation of Intra Ocular Pressure was significantly high ($p < 0.05$). The diurnal variation of Heart Rate and Blood Pressure showed variations from 6AM to 6PM within physiological limits.

Discussion: The diurnal variation of Intra Ocular Pressure, Heart Rate and Blood Pressure in early morning and at evening might be due to the combined homeostatic mechanism of autonomic nervous system and glucocorticoid release.

Conclusion: Hence intra ocular pressure fluctuation more than 30 mmHg during diurnal variation water has diagnostic value towards development of latent Glaucoma.

Keywords: Diurnal Variation, Intraocular Pressure, Blood Pressure, Heart Rate

1. Introduction:

The intra ocular pressure is an essential entity in maintaining the structural and functional integrity of the eye ball. Any abnormalities in the intra ocular pressure of a given eye can result in dysfunction of the eye. The most important factor which regulates the intra ocular pressure within physiological limits is the aqueous humour. Its production and drainage are well governed in order to maintain the shape of the globe and internal circulation of the eye. The intra ocular pressure is maintained by equilibrium between aqueous production from ciliary body and its drainage via trabacular complex. The aqueous humour helps in maintaining the nutrition of the avascular structure of the globe and it also contributes for the refractive state of the eye¹.

The normal intra ocular pressure in humans ranges from 10 to 22 mm of Hg. Anytime if the intra ocular pressure is persistently lower in eye less than 10mm Hg causes ocular hypotony. The persistent rise in intra ocular pressure of the eye more than 22 mm Hg is called ocular hypertension. Both hypo and hypertension have

got adverse effect, like hypotension leads to retinal detachment and shrinkage of eye ball, while increased intra ocular pressure leads to a clinical disease complex known as Glaucoma², where there is insidious and progressive death of optic nerve resulting in permanent blindness of eye (which contributes to 2% of blindness). Hence recording of intra ocular pressure is an important test in the clinical examination of the eye.

In general, the intra ocular pressure is observed, not to be steady throughout the day. It undergoes changes of two different types viz; long term changes and transient changes. The long term changes include the change in the equilibrium between the factors responsible for aqueous production and those governing its escape³. There are mechanisms concerned with the aqueous production, resistance to the outflow facilities and episcleral venous pressure. Disruption in any of these three levels can induce altered new level of intra ocular pressure. Again these factors are re-established to normal when the rate of entry of aqueous humour again equals its elimination rate. In the transient

changes of intra ocular pressure results from alteration in the internal forces acting upon the eyeball and from volumetric changes within the eyeball. During such changes the formation of aqueous differs from the elimination. Those changes are brought about by acts like forcible closure of the eye, blinking, holding of breath⁴. Such changes are very transient and normalcy is attained.

The intra ocular pressure varies in a regular cycle in normal eyes throughout the 24 hours. This variation has been noticed in definitive periodicity. The spikes of elevation have been observed, reaching highest in the early hours of the day. Though this fluctuation is observed they are not noxious and are within normal physiological values. This periodic variability of the intra ocular pressure is considered as normal diurnal variation⁵.

It is observed that the patients showing normal intra ocular pressure in the day time presented with the Glaucoma signs like widening of the cup and typical scotomas in the field. Now when these patients are subjected to screening of intra ocular pressure for 24 hrs presented with rise in intra ocular pressure more than 8-10 mm of Hg from the baseline in the early hours of the day and normal pressure in the day time. Thus, recording diurnal variation in the intra ocular pressure is gaining much significance in diagnosing Latent Glaucoma. Hence the present study was undertaken to investigate the diurnal variation in the Intra Ocular Pressure, Blood Pressure and Heart Rate in healthy individuals.

2. Materials and Methods:

The study was conducted after the institutional ethical clearance and the written informed consent from all the participants. The present study includes 100 healthy male subjects in the age group of 18 – 20 years and who were born and brought up in Gulbarga district with same socioeconomic status. The subjects who are non alcoholic, non-smoking, without any nutritional deficiencies, no refractive errors and free from diseases were included in the study. The subjects with general debilities, Malnutrition, Refractive errors of the eye, Diseases of the eye, Hypertension and Glaucoma were excluded.

Detailed history, name, age, sex, occupation, and personal history, personal habits of the subjects were noted. Family history of hypertension, diabetes, refractive errors and Glaucoma were enquired. This is followed by the measurement of Intra ocular pressure, Heart rate, Systolic

blood pressure and diastolic blood pressure using standard procedures.

The intra ocular pressure was measured by using Schiotz's tonometer. Before measuring the Intra ocular pressure surface anaesthesia was done using 4% lignocaine in both the eyes. Prophylactic antibiotic ciprofloxacin eye drops was installed in both the eyes to prevent infections after each measurements with tonometer. Care was taken not to touch the tip of the dropper.

The heart rate was measured using ECG. The rate was measured by noting the time interval between two R – R waves in lead II. Six to eight R– R complexes were recorded in each setting. Heart rate was calculated by counting number of small squares between two R – R intervals divided by 1500. The systolic blood pressure and diastolic blood pressure was recorded using sphygmomanometer. Pulse pressure and mean arterial pressure calculated using Systolic and diastolic blood pressure.

To measure the diurnal variation in intra ocular pressure on first day the intra ocular pressure was measured from 6.00 AM to 6.00 PM with an interval of every two hours. Six readings were taken for each subject. The heart rate and systolic blood pressure, diastolic blood pressure, pulse pressure and mean arterial pressure were measured from 6.00 AM to 6.00 PM with an interval of every two hours.

2.1 Statistical analysis: The data collected was represented as Mean \pm S.D. and was subjected to statistical analysis by one way ANOVA using SPSS Version- 12. P value less than 0.05 was considered the level of significance.

3. Results:

The Mean \pm SD of age, height and weight was 19.07 \pm 0.83, 169.03 \pm 5.77cms and 52.3 \pm 5.59 kgs respectively. The Body Surface Area, Body Temperature, Respiratory Rate and Urine Output was 1.59 \pm 0.053m², 37.22 \pm 0.02°C, 15.23 \pm 1.89 rate/min and 684.17 \pm 89.12 ml/2hours respectively (Table-1). This indicates that all the subjects are young and healthy.

The diurnal variation of Heart Rate and Systolic Blood Pressure, Diastolic Blood Pressure, Pulse Pressure and Mean Arterial Pressure is represented in Table-2. It shows that the lowest heart rate was recorded early in the morning at 6.00 AM (69.26 \pm 7.42 bpm) and highest heart rate was in the evening at 4.00 PM (78.66 \pm 10.17 bpm). This difference was statistically significant (p<0.05). Similarly, Blood Pressure

also showed a significant variation in the morning and evening (Table-2). Diurnal variation in the Intra Ocular Pressure of both right and left eye was shown in Table-3. It is observed that the diurnal variation in the Intra Ocular Pressure of both right eye and left eye are almost following the similar linear relationship. The diurnal variation of Intra Ocular Pressure in both right eye and left eye was more at 6.00 AM and falls from 6.00 AM to 12:00 noon is almost 2.9 mm Hg and from noon it decreases further in the evening till 6:00 PM with a difference of 1.86 mm Hg. From evening 6:00 PM to morning 6.00 AM there is increase in intra ocular pressure of about 4.78 mm Hg. This variation at different time intervals was statistically significant ($p < 0.05$).

4. Discussion

Over the course of the day, intra ocular pressure varies an average of 3-6mmHg in normal individuals and more in early morning⁶. Patients with glaucoma have much swings of intra ocular pressure that can reach 30mmHg or even 50mmHg in rare cases⁷. Most of the diurnal pressure variation is caused by fluctuations in the rate of aqueous humor formation. The rate of aqueous humor formation falls to low levels during sleep and increases during the day, most likely in response to circulating catecholamines^{8,9}. Some workers postulated that the diurnal intra ocular pressure variation follows the diurnal Glucocorticoid cycles, With intra ocular pressure peaking about 3-4hr after plasma cortisol¹⁰. A modified diurnal curve which is easy to measure an office diurnal curve, where intra ocular pressure measured from 8 am to 6 pm with interval of every 2hr. Pressure swings of 6-8mmHg is common.⁶ Circadian rhythm of intra ocular pressure were shown in young adults with peaks occurring in late dark period¹¹. The various factors responsible for the diurnal variation in IOP include Cardio vascular Factors, Postural variation, neural factors, Hormonal factors, Refractive error, Food and personal habits.

In our study, we observed that, the percentage rise of intra ocular pressure is more in the evening observations in both right and left eyes. The observation may be due to the basal pressures in the morning is high hence percentage rise is low when compared to evening rise of the same eye as the basal pressure is low. We also found that intra ocular pressure is maximum at early morning 6.00 AM

and drops in the evening at 6.00 PM and again rises in early morning before awake.

According to Duke – Elder (1952)¹² the magnitude of the diurnal variation in normal eyes varies individually, being imperceptible in a few and involving an excursion of 3-4 mm Hg in many and exceeding 5 mm Hg in minority. In the present study the diurnal variation of intra ocular pressure in normal healthy eyes is 4.8 mm Hg which is almost nearer to Duke –Elder (1952)¹² and Moses RA (1965)¹³. So with the help of present study and studies carried out on Glaucomatous eyes by Drance (1960)¹⁴ and Duke – Elder (1952)¹² one can conclude that the magnitude of diurnal variation in intra ocular pressure depends largely on the facility of outflow of aqueous humor, if facility is good alteration in secretion rate are reflected in intra ocular pressure changes to a lesser degree than if it is poor, so that while in the normal diurnal variation in intra ocular pressure is only 3 – 4 mm Hg while in glaucoma it may be much greater.

The early morning rise in intra ocular pressure and fall of intra ocular pressure in the evening may be due to the least sympathetic discharge during morning and greatest in the evening. Hence we can conclude that the autonomic nervous system have some role on intra ocular pressure¹⁵. It was found by earlier authors that daily corticosteroid cycle has an influence on diurnal variation of intra ocular pressure. Some drugs have inhibitory effect on adrenocortical biosynthesis, which is associated with decreased intra ocular pressure. Like many biological parameters the intra ocular pressure is subjected to cyclical fluctuations throughout the day. Amplitude greater than 10 mm Hg is considered to be pathological. If intra ocular pressure exceeds above 30 mm Hg during diurnal variation it is considered to be glaucomatous⁵⁶. The obvious primary clinical value of measuring diurnal variation of intra ocular pressure is to avoid the risk of missing a pressure elevation with single readings. In addition patient with intra ocular pressure peak of 6 mm Hg or above in the day time average are more likely to have progressive visual field loss than those with lower amplitude of diurnal fluctuations¹⁶.

With respect to cardiovascular parameters, the diurnal variation in heart rate from morning 6.00 AM to 6.00 PM a quite fluctuating variation of the heart rate was found every two hour interval. It may be due to combined effect of autonomic nervous system and release of glucocorticoids. As we know that least sympathetic activity is

associated with the lowest level of cortisol secretion as well as the least activity of hypothalamic pituitary adrenocortical axis. Similarly the peak heart rate at 4.00 PM may be explained due to the maximum sympathetic activity along with highest cortisol secretion associated with highest activity of hypothalamic pituitary adrenocortical axis¹⁵. In case of systolic blood pressure, diastolic blood pressure, pulse pressure and mean arterial pressure reflects the same diurnal variation as in case of heart rate. All the blood pressure values are least in the morning 6.00 AM and highest in the evening 4.00 PM. The combined effect of autonomic nervous system and hypothalamic pituitary adrenocortical axis can be taken into consideration.

Conclusion:

Though the variation in intra ocular pressure is physiological, IOP fluctuation more than 30 mmHg during diurnal variation has diagnostic value towards development of latent Glaucoma.

References:

1. Becker Shaffer's Diagnosis and therapy of Glaucomas. 7th edition 1999 Page No. 20 to 26.
2. Becker B: The Effect of hypothermia on aqueous humor dynamics: III. Turnover of ascorbate & sodium .Am J ophthalmol 51: 1961;1032.
3. Bonting SL, Becker B. Studies on sodium – potassium activated adenosine triphosphate. XIV. Inhibition of enzyme activity and aqueous humor of flow in the rabbit Eye after injection of Oubain. Invest ophthalmol 3:1964; 523-527.
4. Holland MG, Gipson CC: Chloride ion transport in the isolated ciliary body, invest ophthalmol 9:1970; 20-27.
5. Bito LZ, Davson H: Steady state concentration of potassium in the ocular fluids. Exp Eye Res 3: 1964;283-286.
6. David R. Diurnal Intra Ocular pressure variation: an analysis of 690 diurnal Curves, Br. J ophthalmol 76: 1992; 280-289.
7. Ne Well FW, Krill AE: Diurnal tonography in normal and glaucomatous eyes; Trans Am ophthalmol Soc 62: 1964; 349- 354.
8. Reiss GR. Aqueous humor flow during Sleep. Invest ophthalmol Vis sci 25: 1984; 776-780.
9. Topper JE, Brubaker RF: Effects of Timolol, Epinephrine and aceta zolamide on aqueous humor flow during sleep. Invest ophthalmol Vis sci 26: 1985; 13-15.
10. Weitzman ED .Co-relative 24hours relationship between intra-ocular pressure and plasma cortisol in normal subjects and patients with Glaucoma. Br. J. Ophthalmol 59: 1975; 566-569.
11. Liujh, Kripke, DH, Hollman RE etal. Nocturnal evelation of intra ocular pressure in young adults. Invest ophthalmol vsi sci 39 (13), 1998; 207-12.
12. Duke-elder. Phasic Variation in the ocular tension in the ocular tension in primary glaucoma” Amer Ophthal, 35, 1952; 324-328.
13. Moser R.A. Quoted in “Adler’s physiology of the eye 1965 VII, edn P. 227-254.
14. Drance, Trans, Canad, ophthalo Soc 23, 131, 1960 in System of ophthalmology, Vol. IV. By Ducke Elder 1968. P 278.
15. William F Ganong MD. Review of medical physiology 20th Edition,Mc Graw Hills Publication, Page 219-223 and 565-587.
16. Zeimer, RC, Wilensky, JT, Gieser, DK, Viana, MAG: Association between intra ocular peaks and progression of visual field loss. Ophthalmology 98: 1991; 64-68.

Table – 1: Anthropometric and other physiological parameters recorded from normal male healthy subjects.

Sl.No	Parameters	Value (n=100)
1	Age (Yrs)	19.07 ± 0.83
2	Height (in cms)	169.03 ± 5.77
3	Weight (in Kgs)	52.83 ± 5.59
4	Body Surface Area (m2)	1.599 ± 0.053
5	Body Temperature (°C)	37.22 ± 0.20
6	Respiratory Rate (per min)	15.23 +1.89
7	Urine Output (ml per 2 Hrs)	684.17 ± 89.12

N=100. Values are expressed as Mean ± Standard deviation.

Table – 2: Diurnal variation of Heart Rate and Blood Pressure in normal healthy male subjects recorded at every 2 Hrs of interval.

PARAMETER	6.00 AM	8.00 AM	10.00 AM	12.00 NOON	2.00 PM	4.00 PM	6.00 PM
HR (bpm)	69.26±7.42	76.2±6.64	72.1±6.56	73.3±5.97	74.6±5.68	78.66±10.7	74.56±8.60
SBP(mm Hg)	114±8.7	117±7.89	120±7.61	123±7.23	125±7.48	120±7.67	117±7.89
DBP(mm Hg)	75.3±6.51	75.7±6.06	76.4±5.9	76.7±5.52	77.1±5.38	76.4±5.9	75.7±6.06
PP (mm Hg)	39.1±5.62	41.5±5.12	43.5±4.58	46.6±4.21	47.9±4.53	43.5±4.58	41.5±5.12
MAP (mm Hg)	88.31±6.8	89.49±6.27	90.9±6.15	92.26±5.81	93.04±5.77	90.88±6.5	89.48±6.27

N=100. Values are expressed as Mean ± Standard deviation.

Note: The diurnal variation of HR, SBP, DBP, PP and MAP was lowest early in the morning at 6.00 AM and highest heart rate was in the evening. This difference was statistically significant ($p < 0.05$).

Table – 3: Diurnal variation of IOP (mmHg) of right and left eye in normal healthy male subjects recorded at every 2 Hrs of interval.

IOP	6.00 AM	8.00 AM	10.00 AM	12.00 NOON	2.00 PM	4.00 PM	6.00 PM
RIGHT EYE	20.70 ±1.50	17.31 ± 1.23	17.17 ±1.32	17.83 ±1.49	17.34 ± 1.18	16.95 ±1.18	16.18 ±1.37
LEFT EYE	20.81 ±1.42	17.26 ±1.27	17.17 ±1.32	17.89 ± 1.64	17.34 ± 1.18	16.89 ± 1.03	16.03 ±1.25

N=100. Values are expressed as Mean ± Standard deviation.