Diurnal Variation of Intraocular Pressure in Normal and Ocular Hypertensive Subjects of China

Pages with reference to book, From 171 To 174

Xiao Rong Xi, Xiang Dong Wu, Yang Bin Huang, HuiJuan Lu, Ekhtiar Shiarkar (The School of Basic Medical Sciences, Shanghai Medical University, Shanghai, People's Republic of China.)
Imran Ahniad Queshi (Department of Physiology, Rawalpindi Medical College, Rawalpindi.)

Abstract

This study evaluated the distribution of Intraocular pressure (lOP) levels in 67 normal and 59 ocular hypertensive (OHT) subjects during the day after placing control on all those factors that can affect lOP. The lOP was measured with the Goldmann applanation tonometer. All the subjects were examined according to standard protocols. Both in the normal and OHT subjects, the peak of mean lOP appeared in the morning when the subjects woke up and the trough of mean IOP occurred between 2 a,m. to 4a.m. The mean diurnal variation ware (meanjsem) 2,9±0 .7 and 3.5±0.7 mmHg in the normal and in OHT subjects, respectively. Ninety-four percent of the normal subjects and sixty-eight percent of the OHT subjects exhibited a similar diurnal behaviour in both eyes. The lOP variation did not correlate with the variations of blood pressure. The diurnal variation of IOP,found in Chinese,islowerthan in othernations. The clinical importance of findings that the peaks of lOP occur in the early morning, raised a serious question as to the necessity of extending the diurnal lOP curves beyond the usual working time (JPMA 46:171, 1996).

Introduction

Maslenikwo[1] first described the diurnal variation of intraocularpressure (IOP) in 1904. lOP is subject to chronobiological rhythms similar to other physiological values in the human body, such as body temperature, heart rated blood pressure and hormone secretion. Many investigators[2,3] ,3 have postulated that the diurnal variation does not usually exceed 3-6 mmHg in normal eyes. There are conflicting reports in the literature, however, as to the time of the day at which the peak lOP occurs during the lOP curves. Weitzman et al[4] described the 24-hour pattern of lOP in normal subjects with measurements made hourly. They reported that the lowest ocular tension occurred between 2 and 4 a.m., with the subsequent rise taking place during the later third of the night's sleep. Zeimer et al[5] considered that the momentary lOP elevation is associated with wakening. In contrast to this, other investigators have shown that lOP was highest at 2 p.m[2]. Most of the previous studies have several drawbacks. In recent years it has been noted that intraocular pressure is a dynamic function and is subject to many influences both acutely and over the long term. Many investigators have reported that lOP varies with sex[6] and seasons[7]. It has been reported that drinking water, coffee or alcohol before measurement of lOP has a significant effect on it[8]. Acute hyperglycaemia decreases[9], while chronic hyperglycaemia as in diabetes, increases IOP[10]. Several studies have shown that intraocular pressure is positively correlated with systemic blood pressure[11]. Moreover, racial differences[12] and environmental conditions[13] also have a significant influence on IOP.

After placing control on all the above mentioned lOP influencing factors, this study was planned to evaluate the distribution of lOP levels, during the day, in the normal and ocular hypertensive (OHT) subjects of Shanghai, the largest city of People's Republic of China.

Patients and Methods

All experimental procedures adhered to the Declaration of Helsinki of the World Medical Association. The sample of present study consisted of 67 healthy and 59 OHT subjects with a mean age of 32±S.D. 7 years and 38±S.D. 9 years respectively. All were males. No OFIT subject was taking any medicine. History concerning previous ocular diseases, presence of diabetes mellitus and the occurrence of glaucoma in the family was taken. The criteria for inclusion were absence of any bistozy of eye surgexy and diabetes, normal body temperature and blood pressure. Subjects were asked not to smoke or drink and have a complete rest atleast 30 minutes before the measurement of lOP. The OHT subjects had atleast three TOP readings equal to or greater than 22 mmHg, but nonnal visual fields and normal optic nerves without evidence of asymmetric cupping. To avoid the seasonal variations, this study was conducted only in winter. The subjects were asked to live in the hospital during the three days of examination. The blood pressure was taken in sitting position. After installation of 0.25% fluorescein and 0.4% benoxinate hydrochloride (Fluress) eye drops, the IOP was measured with the Goldmann applanation tonometer (Goldmann Topocon, Germany), first in the right eye and then in the left. The measuring drum was turned until the innerborders of the fluorescein rings (adjusted for equal size) just touched each other at the midpoint of the ocular pulse and the overlap and separation of the mires with each pulse swing was equidistant from the midpoint on both sides. The measuring drum was not to be observed until this defmed point was reached. Three consecutive readings of each eye were taken. Aftereach reading the tonometerwas 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 would minimize observer bias. After waking, the TOPs were measured immediately, which were repeated after3O minutes, 1 hourand then eveiy three hours till next waking. During the perio4 of these three hours, to minimize the effect of food and water, only in the first hour, subjects were allowed to eat and drink. Before each measurement, the subjects took a rest of 30 minutes in supine posture.

Statistical Analyses.The mean of the three readings was computed separately for each eye. Intraocular pressures were measured in whole numbers, but for statistical accuracy, the mean values have been expressed up to one decimal point. For all variables descriptive statistics (mean, standard deviation, standard error of mean) were calculated by Statistical Analysis System 76[14]. All data are expressed as mean and standard error of the mean. Analysis of variance (ANOVA) was used to compare results between different times. Differences are regarded as significant when the P value was less thn 0.05. Actual P values are given where appropriate.

Results

Intraocular pressure determined for 24 hours are shown in Figure 1.

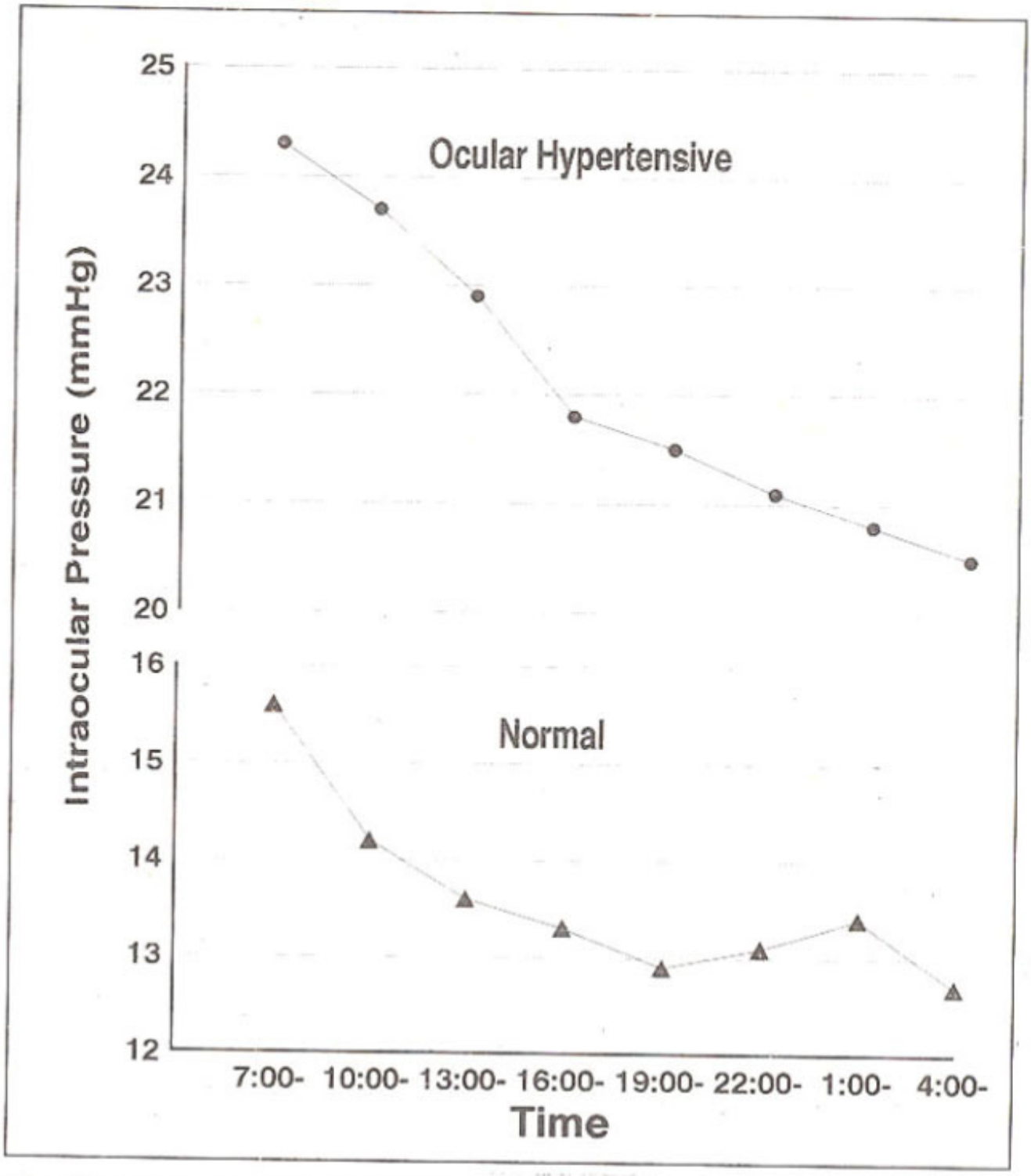

Figure 1. Mean IOP recorded at various times in ocular hypertensive ( ) and normal ( ) subjects.

Both in the normal subjects and OHT subjects, the peak mean IOP appeamd in the morning when the subject woke and the trough of mean lOP occuffed at 2 a.m. to 4 a.m.. The diurnal intraocular pressure curves revealed that the lOP peak was 15.6±0.8 mmHg in the normal and 24.3± 1.5 rnmHg in OHT subjects. Whereas, the trough were 12.7±0.6 and 20.8±1.7mmHg in the normal and OHT subjects

respectively. The mean diurnal variation was 2.9±0.5 mmHg (P<0.02) in the normal and 3.5±0.6 mmHg (P<0.01) in OHT subjects. Ninety-fourpercent of normal subjects and sixty-eight percent of OHT subjects exhibited a similar diurnal behaviour in both eyes.

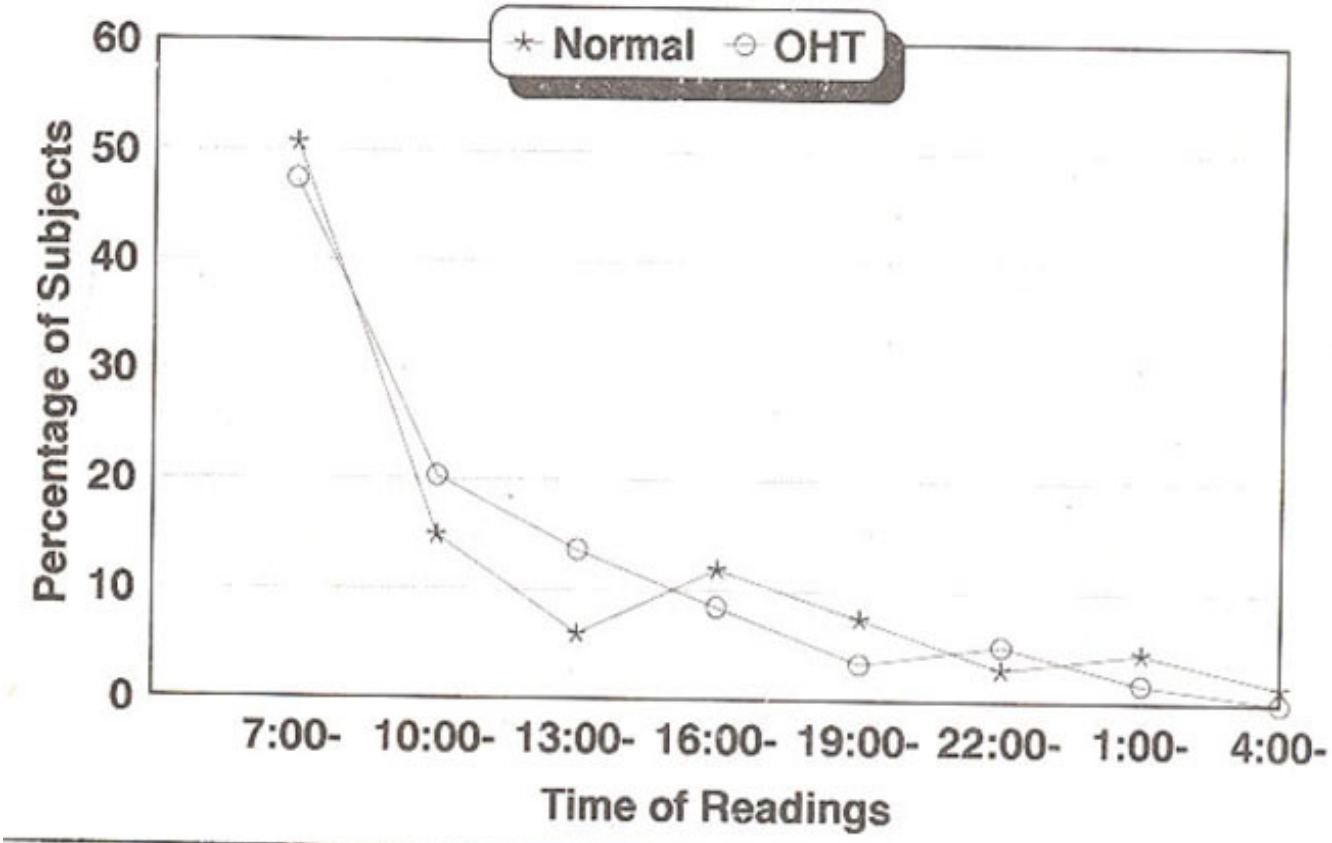

Figure 2. Distribution of subjects according to peaks of IOP at various times. Symbols corresponding to the identification of normal and ocular hypertensive subjects are shown in the upper round frame.

In Figure 2 the distribution of peak lOP reading in the normal and ocularhypertensive subjects, atthe sevendifferent times, is presented. Among the normal subjects, overall 56% of peaks were found on the first earliest lOP measurement in the morning, whereas in the OHT subjects, at the same time, about 58% of peaks were found. The blood pressure of all the subjects was in normal range. The lOP did not correlate with the variation of blood pressure determined alongwith lOP (data not shown).

Discussion

This study demonstrates the lOP peak presents upon waking. Review of previous studies of the diurnal variation in lOP shows considerable variation when compared to the current study[2-5].The difference among studies may be due to various factors. In recent years, it has been noted that intraocular pressure is a dynamic function and is subject to many endogenous influences both acutely and over the long term. The variability in the results of previous studies may be due to negligence of several variables, including sex[6], drinking of water, coffee oralcohol before lOP measurement[8], seasonal variations[7] etc. After taking into account all those factors that can affect intraocular pressure, the diurnal variation of lOP in Chinese, reported by this study, is lower than that in other nations reported by previous studies. The presence of an elevated lOP upon awaking is puzzling. Some investigations suggested a mechanism that could account for both the rise and the decline of lOP. Hormonal

variation[14,15]autonomic or humeral control[16,17] and changes in the vascular tone[18] have been suggested as factors affecting the aqueous outflow. Gloster and Poinoosawmy[19] concluded that one hour in darkness caused an increase in lOP that decreased upon exposure to light. They also pointed out that the dilatation and constriction of the pupil were not the main cause of lOP variations. Brown et al[20] mentioned that malatonin could be involved in the process, but as they point out, the fact that the lOP increases also with sleep, when the melatonin level is presumably low, tends to cast doubts on this explanation. The lOP is expected to be low at night based on the fact that aqueous production is decreased during sleep[21]. Therefore, it seems that the elevated IOP is related to sleep close to the time of awaking orto the wakening process itself. The sudden rise in blood pressure has been reported to occurupon waking[22]. This could cause an increase inocular blood volume, mostly in the choroid and thereby lead to an increase in lOP. This pressure peak would only be momentaiy because it would decrease with time due to flow of aqueous out of the eye and/or regulatory vascular mechanisms[5]. In ocular hypertensive subjects, if the decline is mainly governed by outflow, the time decay can be expected to be in the range of tonographic decay, which is approximately 10 mrnHg in 4 minutes for lOPs, between 20 and 30 mmmHg[23]

It is commonly believed that there is a fair degree of symmetry between fellow eyes[24]. In the current study, a considerable prevalence of differences in the diurnal lOP pattern between the two eyes of ocular hypertensive and normal person has been noted. This suggests that factors specific to each affected eye may interfere with systemic regulatoiy components and thus play an important role in determining the lOP.

The diurnal lOP variation, a physiological rhythm, is essentially a metabolic cycle synchronized with the external periodicity of day and night through the influence of variations in illumination, temperature and other environmental factors, on the nervous and endocrine systems. The existing literature shows the influence of hormones upon intraocular pressure. There is evidence that corticotropin, vasopressin, thyroxin, insulin, glucocorticoids and mineralocorticoids play a role in the physiologic regulation of intraocular pressure. Growth hormone, progesterone, estrogen, chorionic gonadotropin and relaxin may influence intraocular pressure when administered in pharmacologic doses. Some of these hormones increase, while others decrease intraocular pressure[25]. Diurnal changes in intraocular pressure have been correlated with circulating eosinophil levels[26], although this relationship has been challenged by other investigators[27]. Patients with Cushing's syndrome have been reported to have increased diurnal variations of intraocular pressure[28] and conversely, patients with adrenal or pituitaiy insufficiency have shown decreased diurnal variations of intraocular pressure28,29 Linner[29] felt that this was due to a lack of variation in aqueous flow. Correlations between diurnal fluctuations in intraocular pressure and plasma glucocorticoid levels have been found in normal individuals and in patients with glaucoma[30]. There seemed to be a four-hour lag between the peak level of the plasma glucocorticoids and the peak in intraocular pressure[30]. Administration of SU4885, an inhibitor of glucocorticoid and mineralocorticoid synthesis[30] diminished the diurnal fluctuation of intraocular pressure[31]. Alterations in the mucopolysaccharide content of the anterior chamber or the trabecular tissues have been noted after administration of glucocorticoids by some investigators21. while other investigators failed to find this alteration[32]. Radnot[33] noted that unilateral adrenalectomy in rabbits decreased intraocular pressure on the ipsilateral side. Bilateral adrenalectomy decreased intraocular pressure and aqueous flow[34]. Insummary, itwouldappearthat endogenous glucocorticoids may play a role in the physiologic regulation off lOP through aqueous inflow and perhaps aqueous outflow. Pharmacologic doses of glucocorticoids affect both facilities of outflow and aqueous inflow, although it is unknown whether this is a direct effect of the glucocorticoids or a secondary effect. In one review, Waitzmar concluded that the hypothalamus might be the major central nervous system

controlling site for changes in IOP. Certainly, the 24-hour correlative relationships with differing hypeth2larnic controlled circadian events, such as neuroendocrinc processes, body temperature, sleep-waking functions and autonomic activity would support that this central nervous system area may be critically involved[35]

We realize that starting the diurnal variation curve of IOP in the clinic around 8 am. is less than ideal, because the highest lOP occurs immediately after waking. It is also possible that the home tonometry, as advocated by Zeimer[36], covers a larger portion of the 24 hour cycle. Nevertheless, the widely employed practice today is IOP measurement by ophthalmologists in their offices and therefore, the information collected and presented here is still useful. The clinical importance of ourfinding, that the peak lOPs occur in the early morning, raised a serious question as to the necessity of extending the diurnal lOP curves beyond the usual working time. More important, it emphasises the fact that solitaiy lOP examination taken in the afternoon may miss most of IOP peaks. This finding indicates that a revision of the timetable for lOP examination in the ocular hypertensive patients may be warranted.

References

1. Maslenikwo, A. Ucber Thgseschwankungcn des intraokularen druckes bei glaukom. Z. Augenheilkd., 1904;11:564-570
2. Kitazawa, V. and Horie, T. Diurnal variation of intraocular pressure in primary open angle glaucoma. Am. J. Ophthalmol., 1975;79:557-566.
3. David, R., Zang will, L., Briscoc, D.ctal. Diumal intraocular pressure variations: An analysis of 690 diurnal curves. Br. J. Ophthalmol., 1992;76:280-283.
4. Weitzman, E.D., Henkind, P., Leitman, M. et al. Correlative 24 hour relationships between intraocular pressure and cortisol in normal subjects and patients with glaucoma. Br. J. Ophthalmol., 1975;59:566-572.
5. Zeimer, R.C., Wilensky, IT. and Gieser, D.K. Presence and rapid decline of early morning intraocular pressure peaks in glaucoma patients. Ophthalmol., 1990;97:547-550.
6. Colton, T. and Ederer, F. The distribution of intraocular pressure in the general population. Surv. Ophthalmol., 1989;25:123-9.
7. Blumenthal, M , Blumenthal, R. and Penitz E. Seasonal variations in intraocular pressure. Am. 3. Ophthalmol., 1970;187:137-40.
8. Buckingham, T. and Young, R. The rise and fall of intraocular pressure: The influence of physiological factors. Ophthalmic. Physiol. Opt., 1986;6:95-99.
9. Ponosawmy ,D. and Winder, A.F. Ocular effect of acute hyperglycaemia. Br. 3. Ophthalmol., 1984;68:585-589.
10. Qureshi, I.A. The effects of mild. moderate and severe exercise on intraocular pressure in glaucoma patients. Jpn. 3. Physiol., 1995;45:561-569.
II. Klein, B.E. and Klein, R. Intraocular pressure and cardiovascular risk variables. Arch. Ophthalrnol., 1981 ;99:837.9.
12. Kass, MA.. Zimmerman, T.J., Alton, E. eta!. Intraocular pressure and glaucoma in the Zuni indians. Arch. Ophthalmol., 1978;96:2212-3.
13. Stoupel, E., Goldenfeld, M. Shimshoni, M. et al. Intraocular pressure in relation to four levels of daily geomagnetic and extreme yearly solar activity. Int. J. Biometerol., 1993;37:42-5.
14. Barr. A.i., Goodnight, H., SaIl, J.P. et al. A users guideto SAS 76, Raleigh, SAS institute, 1976.
15. kass, MA. and Sears, ML. Hormonal regulation of intraocular pressure. Surv. Ophthalmol., 1977;22:153-166.
16. Horwich, H., Breinin, G.M. Phasic variations in tonography. Arch. Ophthalmol.. 1954,51:687-694.
17. Kessing, S.V., Gregersen, E. The distended disc in early stages of congenital glaucoma. Acts

Ophthalmol., 1977;55:43 1-435.
18. Dobree, 3.H. Vascular changes that occur during the phasic variations of extension in chronic glaucoma. Br. J. Ophthalmol., 1953;37:293-300.
19. Golsier, J., Poinoosawmy, D. Changes in intraocular pressure during and after the dark-room test. Br. 3. Ophthalmol., 1973,57:170-178
20. Brown, B., Burton, P., Mann, S. eta!. Fluctuations in intra- ocular pressure with sleep: II Time course of lOP decrease after waking from sleep. Invest. Ophthalmol. Vis. Sci., 1984;25:776-778.
21. Reiss, OR., Lee, D.A., Topper, J.E. et al. Aqueous humor flow during sleep. Invest, Ophthalmol. Vis. sci., 1984;25:776-778.
22. Floras, J.s., Jones, 3. V., Johnston, J.A. et al. Arousal and the circadian rhythm of blood pressure. Clin. Sci. Mol. Med., 1978;55 (suppl I)395-397
23. Kloker, A.E. and Hethering, J. eds. Diagnosis and therapy ofthe glaucomas. 5th ed.,St. Louis, C.V. Mosby 1983, pp. 519-535.
24. Wilensky, iT., Gieser, D.K., Dietsche, M.R. eta!. Individual variability in the diurnal intraocular pressure curvc. Ophthalmol., 1993; 100:940-944.
25. Kass. MA., Sears, ML. Hormonal regulation of intraocular pressure. Surv. Ophthalmol., 1977;22:153-66.
26. Stepanik. J. On the pathogencsis of the diurnal variations of the intraocular tension. KIm. Monatsbl. Augenheilkd., 1954;125:737-743.
27. Cambiaggi, A., Spurgen, W.M. and Spurgcn, R. Diurnal changes in eosinophil count. Comparison with changes in intraocular pressure, tonographic valuesand aqueous veins. Arch. Ophthalmol., 1956,55:765-778.
28. Krasnovid, TA. A new hypothesis on the mechanism of diurnal variation in intraocular tension. Oftalmol. Zh., 1966;21 :185-194.
29. Linner, E. The rate of aqueous flow and the adrenals. Trans. Ophthalmol. Soc. U.K., 1959;79:27-32.
30. Boyd. T.A.S. and McLeod, L.D, Circadian rhythms of plasma corticoid levels, intraocular Pressure and aqueous outflow facility in normal and glaucomatous eyes. Ann. N. V. Acad. Sci., 1964,117:597-613.
31 Kasavina, B.S., Pantieleva, V.M and Shapkina, AM. Effect ofglucocorticoids on the eye tissue -mucopolysaccharidcs of rabbits and the state of the ophthalmotone regulation Vestn Oftalmol., 1970:1:13-17.
32. Futa, R. Enzymatic histochemical studies on the angle of the anterior chamber.
33. Effect of local corticosteroid on some enzymes relating to phosphoric acid metabolism. Ada Soc. Ophthalmol. Jap., 1972;76:441-448.
33. Radnot, M. Die, Nebenniere und der intraoculare Druck. Ophthalmologica, 1944;108:137-139.
34. Linnen, E. and Wistrand, P.J. Adrenal cortex and aqueous humour dynamics Exp. Eye Res., 1963;2:148-159.
35. Conroy, R.T.W.L. and Mills, J.N. Human circadian rhythms. London, Churchill, 1970.
36. Zeimer, R.C., Wilensky, J.T., Gieser, D.K. et al. Application of a self tonometer tohometonometzy. Arch. Ophthalmol., 1986;104:49-53.