



Original article

Evaluation of the circadian fluctuations of intraocular pressure and ocular perfusion pressure in different types of glaucoma

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Abstract:**Background:**

Glaucoma is a frequent leading cause of blindness. Objective evidence showed that it can be secondary to optic nerve head hypoperfusion and autonomic dysfunction, not only to ocular hypertension. This makes the assessment of ocular blood flow a crucial step in the management of this disease.

Aim:

To investigate the circadian fluctuations of the intraocular pressure (IOP) and of the mean ocular perfusion pressure (mOPP) in patients with different types of glaucoma.

Materials and methods:

Sixty-five eyes of 65 glaucoma patients, managed in the Ophthalmology Department of the Careggi University Hospital, Firenze, Italy (2012-2014). Among these eyes, 22 had normotensive glaucoma (NTG), 21 hypertensive glaucoma (HTG), and 22 exfoliative glaucoma (XFG). The IOP was measured by Goldmann tonometry and the blood pressure, both systolic (sBP) and diastolic (dBP), by Riva-Rocci sphygmomanometry, at three time points (8am, 2pm, 8pm). The mOPP was then calculated according to the formula $mOPP = [2/3 (2/3 dBP + 1/3sBP) - IOP]$.

Results:

The fluctuations of IOP and mOPP were statistically significant in all the studied eyes ($p < 0.001$ for all the comparisons). Both IOP and mOPP showed significantly larger fluctuations in the XFG eyes than in the NTG and HTG ones ($p < 0.001$ for IOP and $p = 0.001$ for mOPP).

Conclusions:

In our study, the mOPP had larger circadian fluctuations in eyes with XFG than in those with NTG and HTG. This parameter deserves to be assessed in all types of glaucoma.

Key words: Glaucoma, intraocular pressure, mean ocular perfusion pressure.

Introduction:

Glaucoma is currently defined as a chronic progressive optic neuropathy with typical anatomical and clinical features and consequent visual impairment. Other than ocular hypertension, optic nerve head hypoperfusion and autonomic dysfunction are the most relevant physio-pathologic risk factors [1].

The aim of this study is to assess the circadian fluctuations of the intraocular pressure (IOP) and of the mean ocular perfusion pressure (mOPP) in patients with different types of glaucoma.

Materials and methods:

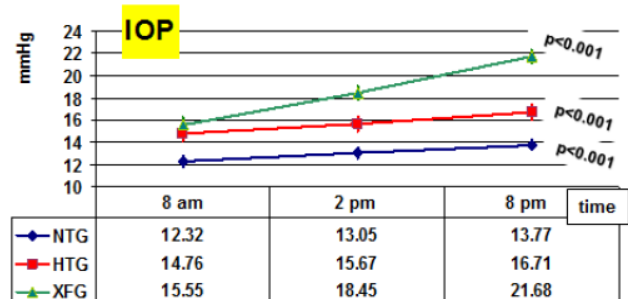
Sixty-five eyes of sixty-five glaucoma patients, referred to the Ophthalmology Department of the Careggi University Hospital, Firenze, Italy in the period 2012-2014 were included in this retrospective study, approved by the local ethic committee. The eyes were divided in three groups: normotensive glaucoma (NTG, n=22), hypertensive glaucoma (HTG, n=21) and exfoliative glaucoma (XFG, n=22). All the selected eyes had normal corneal thickness values and were matched for severity of disease (moderate, GSS 1L-2L) and treatment (prostaglandins eye drops). After the measurement of IOP by Goldmann tonometry and of blood pressures by Riva-Rocci sphygmomanometry, the mOPP was calculated according to the formula $mOPP = [2/3 (2/3 \text{ dBP} + 1/3 \text{ sBP}) - IOP]$, at three time points (8am, 2pm, 8pm). The data were shown as mean \pm standard error of the mean (SEM). The statistical analyses were carried out using SPSS 24.0. The IOP and the mOPP measurements were compared in every studied group by means of ANOVA for repeated measures. A p value <0.05 was set as significant.

Results:

Sex ratio and mean age were as follows:

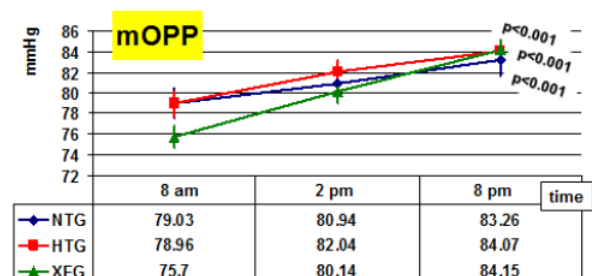
NTG: male (M): female (F)=10:12, mean age 70.0 ± 0.6 years; HTG: M: F=10:11, mean age 70.3 ± 0.6 years; and XFG: M: F=11:11, mean age 71.3 ± 0.9 years.

The IOP and mOPP values significantly varied throughout the day in all the three study groups ($p < 0.001$ for all the comparisons) (figure 1). Both variables showed significantly larger fluctuations in the XFG eyes than in the NTG and HTG ones ($p, 0.001$ for IOP and $p = 0.001$ for mOPP) (figure 2).



| Fluctuations | | | | |
|--------------|-----------------|-----------------|-----------------|-----------|
| | NTG | HTG | XFG | p |
| IOP (mmHg) | 1.46 ± 0.14 | 1.95 ± 0.29 | 6.14 ± 0.42 | < 0.001 |

Figure 1. Diurnal IOP course in the three studied groups (graph, above). Comparison of IOP diurnal fluctuations among the three studied group



| Fluctuations | | | | |
|--------------|-----------------|-----------------|-----------------|-------|
| | NTG | HTG | XFG | p |
| mOPP (mmHg) | 4.45 ± 0.70 | 5.11 ± 0.75 | 8.44 ± 0.91 | 0.001 |

Figure 2. Diurnal mOPP course in the three studied groups (graph, above). Comparison of mOPP diurnal fluctuations among the three studied group (table, below).

Discussion:

Hypertensive glaucoma (HTG), normotensive glaucoma (NTG) and exfoliative glaucoma (XFG) are the most common types of glaucoma [2-5]. They have in common typical optic nerve and visual field alterations, and differ for the weight that various risk factors have in the onset and progression of the disease.

Among the risk factors for glaucoma, high intraocular pressure (IOP) is the most important one, but reduced optic nerve blood supply has a relevant role too.

Elevated IOP is the most evident risk factor for HTG and XFG, but low mOPP has been described as well [6-10]. On the contrary, in NTG IOP is normal by definition, and low mOPP has been considered the main risk factor [11-15].

IOP can be precisely measured by tonometry, while a parameter called mean ocular perfusion pressure (mOPP) is a good estimate of the optic nerve blood supply. This parameter takes into account systemic and diastolic blood pressure (sBP and dBP) measurements and is calculated using the formula: $mOPP = [2/3 \text{ dBP} + 1/3 \text{ sBP}] - IOP$ [16].

Both IOP and mOPP physiologically vary throughout the 24 hours. However, these fluctuations have been reported to be larger in glaucoma subjects than in healthy controls [17,18].

The few published papers have by far suggested that diurnal variations of IOP and mOPP may influence the severity and the progression of glaucoma [19-25].

To date, no clear data about differences in such variations among different types of glaucoma are available. We designed and conducted the following study to contribute to the research on this subject. The assessment of our findings can be more objective on a larger series.

Conflict of interest: none

References:

- [1] Jonas JB, Aung T, Bourne RR, et al. Glaucoma. *Lancet* 2017; 390:2183-93.
- [2] Foster PJ, Buhmann R, Quigley HA, et al. The definition and classification of glaucoma in prevalence surveys. *Br J Ophthalmol* 2002; 86:238-42.
- [3] Anastasopoulos E, Topouzis F, Wilson MR, et al. Characteristics of pseudoexfoliation in the Thessaloniki Eye Study. *J Glaucoma* 2011; 20:160-6.
- [4] Tham YC, Li X, Wong TY, et al. Global prevalence of glaucoma and projections of glaucoma burden through 2040: a systematic review and meta-analysis. *Ophthalmology* 2014; 121:2081-90.
- [5] Kim KE, Park KH. Update on the prevalence, etiology, diagnosis, and monitoring of normal-tension glaucoma. *Asia Pac J Ophthalmol* 2016; 5:23-31.
- [6] Konstas AG, Tsironi S, Ritch R. Current concepts on the pathogenesis and management of exfoliation syndrome and exfoliative glaucoma. *Compr Ophthalmol Update* 2006; 7:143-4.
- [7] Coleman AL, Miglior S. Risk factors for glaucoma onset and progression. *Surv Ophthalmol* 2008; 53 Suppl 1: S3-10.
- [8] Stewart WC, Kolker AE, Sharpe ED, et al. Long-term progression at individual mean intraocular pressure levels in primary open-angle and exfoliative glaucoma. *Eur J Ophthalmol* 2008; 18:765-70.
- [9] Galassi F, Giambene B, Menchini U. Ocular perfusion pressure and retrobulbar haemodynamics in pseudoexfoliative glaucoma. *Graefes Arch Clin Exp Ophthalmol* 2008; 246:411-6.
- [10] Holló G, Quaranta L, Cvenkel B, et al. Risk factors associated with progression in exfoliative glaucoma patients. *Ophthalmic Res* 2012; 47:208-13.
- [11] Caprioli J, Coleman AL. Blood pressure, perfusion pressure, and glaucoma. *Am J Ophthalmol* 2010; 149:704-12.
- [12] Galassi F, Giambene B, Varriale R. Systemic vascular dysregulation and retrobulbar haemodynamics in normal-tension glaucoma. *Invest Ophthalmol Vis Sci* 2011; 52:4467-71.
- [13] Mozaffarieh M, Flammer J. New insights in the pathogenesis and treatment of normal tension glaucoma. *Curr Opin Pharmacol* 2013; 13:43-9.
- [14] Mottet B, Aptel F, Geiser M, et al. Vascular factors in glaucoma. *J Fr Ophthalmol* 2015; 38:983-95.
- [15] Mallick J, Devi L, Malik PK, et al. Update on normal tension glaucoma. *J Ophthalmic Vis Res* 2016; 11:204-8.
- [16] Riva CE, Grunwald JE, Petrig BL. Autoregulation of human retinal blood flow. An investigation with Doppler velocimetry. *Invest Ophthalmol Vis Sci* 1986; 27:1706-12.
- [17] Pemp B, Georgopoulos M, Vass C, et al. Diurnal fluctuations of ocular blood flow parameters in patients with primary open-angle glaucoma and healthy subjects. *Br J Ophthalmol* 2009; 93:486-91.
- [18] Jonas JB, Budde WM, Stroux A, et al. Circadian intraocular pressure profiles in chronic open angle glaucomas. *J Ophthalmic Vis Res* 2010; 5:92-100.
- [19] Werne A, Harris A, Moore D, et al. The circadian variations in systemic blood pressure, ocular perfusion pressure, and ocular blood flow: risk factors for glaucoma? *Surv Ophthalmol* 2008; 53:559-67.
- [20] Sung KR, Lee S, Park SB, et al. Twenty-four-hour ocular perfusion pressure fluctuation and risk of normal-tension glaucoma progression. *Invest Ophthalmol Vis Sci* 2009; 50:5266-74.
- [21] Antal S, Jürgens C, Grossjohann R, et al. Diurnal variation of ocular pressure in open-angle glaucoma with telemonitoring. *Klin Monbl Augenheilkd* 2009; 226:168-75.
- [22] Kim Y, Oh WH, Park KH, et al. Circadian blood pressure and intraocular pressure patterns in normal tension glaucoma patients with undisturbed sleep. *Korean J Ophthalmol* 2010; 24:23-8.
- [23] Jürgens C, Grossjohann R, Tost FHW. Relationship of systemic blood pressure with ocular perfusion pressure and intraocular pressure of glaucoma patients in telemedical home monitoring. *Med Sci Monit* 2012; 18:MT85-9.
- [24] Quaranta L, Katsanos A, Russo A, et al. 24-hour intraocular pressure and ocular perfusion pressure in glaucoma. *Surv Ophthalmol* 2013; 58:26-41.
- [25] Spaniol K, Schöppner M, Eter N, et al. Diurnal fluctuations of intraocular pressure, blood pressure, and ocular perfusion pressure in glaucoma patients. *Klin Monbl Augenheilkd* 2015; 232:773-8.