Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/m41tp569

Mean Ocular Perfusion Pressures Circadian Fluctuation and Its Relationship with different types of Glaucoma

Palaboina Rupanjali Yadav[1*], Narayan.M[2]

[1*]Post Graduate Student, Department of Ophthalmology, PESIMSR, Kuppam
[2]HOD, Department of Ophthalmology, PESIMSR, Kuppam

***Corresponding Author:** Palaboina Rupanjali Yadav
* Email Id- rupayadav353@gmail.com

ABSTRACT

Purpose: This study investigates the circadian fluctuation of mean ocular perfusion pressure (MOPP) and its association with different types of glaucoma, aiming to determine its role in disease pathophysiology and progression.

Methods: A cohort of patients diagnosed with primary open-angle glaucoma (POAG), normal-tension glaucoma (NTG), and angle-closure glaucoma (ACG), along with age-matched controls, were assessed. Intraocular pressure (IOP) and systemic blood pressure (BP) were recorded at multiple time points over a 24-hour period to calculate MOPP. Circadian variations and their correlations with glaucoma severity were analyzed.

Results: Significant circadian fluctuations in MOPP were observed across all groups, with the lowest values occurring during nighttime. Patients with NTG exhibited the most pronounced reductions in nocturnal MOPP compared to POAG and ACG. Greater MOPP variability was associated with more severe visual field loss, particularly in NTG and POAG cases.

Conclusion: Circadian MOPP fluctuations appear to play a crucial role in glaucoma pathogenesis, with NTG patients being most susceptible to nocturnal reductions. Monitoring and stabilizing MOPP variations may be essential in optimizing glaucoma management and preventing disease progression.

1. INTRODUCTION

1.1 BACKGROUND

Glaucoma is a chronic and progressive optic neuropathy that is still one of the main causes of irreversible blindness globally. This is mainly characterized by progressive loss of retinal ganglion cells resulting in loss of vision field. Despite elevated intraocular pressure (IOP) being the most documented and consistent modifiable risk factor over the last 150 years, many clinical observations draw attention to the non-allergy response to repetitive exposure to the same antigen even in the case of normal IOP. This indicates that other contributing mechanisms exist in addition to elevated IOP alone.

Among them, one such important variable is the contribution of the blood to the optic nerve head that is highly dependent on a balance between systemic blood pressure and IOP. The balance is given in quantitative terms by the mean ocular perfusion pressure (MOPP). Note: MOPP is an indirect measure of blood volume supplied to the optic nerve and retina. Excessively low MOPP may result in ischemic injury to the optic nerve and thus hasten glaucomatous degeneration.

Well, MOPP is affected by not only global circulatory values but also by ocular pressure-volume dynamics. The formula utilized to calculate it incorporates systolic blood pressure (SBP), diastolic blood pressure (DBP) and IOP. The typical formula used is:

$$\text{MOPP} = \frac{2}{3}[\text{DBP} + \frac{1}{3}(\text{SBP} - \text{DBP})] - \text{IOP}$$

This equation illustrates how decreased systemic blood pressure and increased IOP can serve to reduce ocular perfusion. Both blood pressure and IOP have circumferential rhythms, that is, their values rejoinder throughout 24-h of time. Blood pressure usually drops overnight while IOP stays stable or even increases slightly in some people. This can potentially lead to a decrease in MOPP during the night, particularly in susceptible individuals like patients with normal-tension glaucoma (NTG).
Recent investigations have postulated that circadian rhythms of MOPP, with localized MOPP reductions occurring at night-time, may play an important role in the pathogenesis/open-angle glaucoma and its progression. What has remained less well-studied is the degree of these fluctuations and how they may differ between different modes of glaucoma (e.g. primary open-angle glaucoma (POAG), NTG and angle-closure glaucoma (ACG)). These differences may lead to novel approaches to individualized treatment of glaucoma with a focus on enhancing and stabilizing ocular blood flow in addition to IOP, particularly at night when the eye may be at greatest risk.

1.2 GLAUCOMA AND PERFUSION PRESSURE

Glaucoma is not a single condition but rather a collection of diseases characterized by the result of progressive optic nerve damage. Of its main subtypes, three can be considered the most studied Primary Open-Angle Glaucoma (POAG), Normal-Tension Glaucoma (NTG), and Angle-Closure Glaucoma (ACG). Though each of those conditions has specific etiologies and presentations, they are all susceptible to variations in ocular perfusion pressure.

In POAG, which is the most prevalent subtype of glaucoma, the drainage angle of the eye is open, however, there is a increased outflow resistance to aqueous from the anterior chamber, causing a gradual increase in IOP. This constant pressure eventually harms the optic nerve. Nevertheless, it has been appreciated increasingly that the POAG population may also have vascular dysregulation, such as reduced impairment autoregulation of blood flow and hyper/hypo trophic perfusion pressures at night.

Normal-Tension Glaucoma (NTG) is especially interesting because patients exhibit glaucomatous optic neuropathy even reaching statistically normal IOP values. This subtype implicates the non-IOP-related factors most prominently the vascular insufficiency. Previous research has indicated that patients with NTG often have nocturnal hypotension that results in substantial reductions in MOPP during the night. These perfusion deficits can rob the optic nerve of oxygen and nutrients at the most vulnerable of times, promoting nerve fiber loss, even when IOP is not elevated.

On the other hand, Angle-Closure Glaucoma (ACG) is due to anatomical defects that inhibit outflow of aqueous humor leading to acute or intermittent elevations in IOP. Although perfusion pressure disturbances may be a secondary consideration in this disorder, rapid rises in IOP can still elicit acute perfusion deficits which endanger the optic nerve.

Circadian variation further complicates the interaction between BP, IOP and MOPP. The ocular perfusion pressure is probably at its most risk of dropping to critically low levels at night when systemic blood pressure tends to fall and IOP may not decrease or may even be above the daytime value. In patients with poorly or innervated vascular autoregulation, this gap puts even greater strain on the optic nerve.

Thus, changes to MOPP throughout the day and the association of these changes with different glaucoma subtypes could inform on the underlying mechanisms of disease. It may also help in identifying patients who are at the highest risk of progression even if clinically stable during the day and other aspects that can help prediction of the disease. This creates a strong argument for considering the inclusion of MOPP monitoring during a full glaucoma assessment, and reinforces the need for personalized treatment strategies based on vascular health aside IOP.

1.3 STUDY RATIONALE

Despite representing the bedrock for the diagnosis and treatment of glaucoma, the absence of disease progression in some patients with treated or normal IOP presents an opportunity to search for alternative players not least, ocular perfusion pressure. Hourly fluctuations in ocular perfusion pressure and low mean ocular perfusion pressure (MOPP), especially at night, have been proposed in numerous studies to cause retinal ganglion cell death from ischemic mechanisms. Yet the details of how MOPP varies across circadian time, and how closely this variation correlates with the severity of different types of glaucoma remain far from certain.

However, blood pressure and IOP are usually measured at office hours in clinical practice. Such daytime recording will miss important night-time changes, including physiological dips in blood pressure or unrecognized surges in IOP that can significantly reduce the perfusion pressure. Such a limitation is specifically important for Normal-Tension Glaucoma (NTG) patients who might have an important nocturnal drop of MOPP even when their IOP remains normal diurnally. Similarly, patients of Primary Open-Angle Glaucoma (POAG) and Angle-Closure Glaucoma (ACG) may have detectable, but unmeasured, perfusion pressure abnormalities.

Thus, the underlying rationale of this study is based on enhancing our understanding of MOPP circadian behavior and how that relates to glaucoma pathogenesis. The current study compares MOPP fluctuations in POAG, NTG, ACG, and age-matched healthy controls to better determine whether perfusion instability is a common or distinct risk factor among glaucoma types.

The study also aims to determine if more variability in MOPP, in particular drops at night, is associated with worse visual field loss or optic nerve damage. Recognizing these patterns might enable more personalized vigilance strategies, with tailored treatment with 24-hour IOP and BP recording or therapeutic interventions at night.

1.4 OBJECTIVES OF THE STUDY

This study aimed to assess the 24-hour variations in mean ocular perfusion pressure (MOPP) between normal controls, patients with primary open angle glaucoma (POAG), and normal tension glaucoma (NTG).

- To compare the magnitude and chronology of MOPP changes in patients with POAG, NTG, ACG, and healthy controls.
- To evaluate the association of fluctuation of MOPP with severity of glaucomatous damage.
- To emphasize the clinical relevance of nighttime MOPP measurement in the management of glaucoma
- By addressing these objectives, the study aspires to advance a comprehensive glaucoma perspective beyond intraocular pressure to advance the diagnosis and treatment of glaucoma.

2. LITERATURE REVIEW

2.1 UNDERSTANDING MEAN OCULAR PERFUSION PRESSURE (MOPP)

MOPPM has recently become one of the most important contributed physiological measurements to this vascular theory of glaucomatous optic neuropathy. Mean ocular perfusion pressure (MOPP) represents a pressure gradient that drives blood to the optic nerve and retina, and is the difference

between systemic blood pressure and intraocular pressure (IOP). The most common calculation is the following:

$$\mathrm{MOPP} = \frac{2}{3}[\mathrm{DBP} + \frac{1}{3}(\mathrm{SBP} - \mathrm{DBP})] - \mathrm{IOP}$$

Since then, vascular theories of glaucoma have gained growing acceptance (Flammer and Mozaffarieh, 2008), as recent publications suggest that a lower perfusion pressure both as a chronic state or even a variable one may disturb the circulation in the optic nerve head to contribute to the glaucomatous damage. Subsequent studies demonstrating the link between low MOPP and the progression of visual field defects, especially in the case of normal-tension glaucoma (NTG) propelled this hypothesis into popularity (Choi & Kook, 2015; Costa et al., 2014).

Systemic blood pressure, IOP, and therefore MOPP are not constant but are influenced by circadian changes. Physiologic "nocturnal dip" in blood pressure—normal for most—is a potential risk for lower MOPP during the night, especially along with increased or unchanged IOP at night. According to Charlson et al. This lack of match poses a significant risk for patients with glaucoma associated with impaired vascular autoregulation (Khaing et al.2014).

2.2 CIRCADIAN RHYTHMS IN IOP, BP, AND MOPP

The circadian rhythm of IOP and BP has been studied in several healthy people and glaucoma patients. Liu et al. (2003) showed that IOP is highest in the predawn hours and stabilizes throughout the course of the day, while systemic blood pressure declines at night, a pattern termed nocturnal dipping. It is well documented that sleep is associated with a decline of MOPP that creates a "high-risk window" where MOPP will be at dangerously low values, hence predisposing to optic nerve ischaemia (Gherghel et al., 2004).

Grieshaber et al. (2007) found NTG patients to have exaggerated nocturnal dips in BP, resulting in greater reductions in MOPP in NTG than POAG patients. Similarly, Bowe et al. They reported that MOPP drop of over 10 mmHg at night increased the risk of visual field progression in a multi-racial population independent of IOP.

2.3 GLAUCOMA SUBTYPES AND VASCULAR DYSREGULATION

Reduced MOPP has been associated with increased optic nerve damage progression (Leske et al., 2008); however, in Primary Open Angle Glaucoma (POAG), vascular dysregulation runs in parallel with increased IOP. Conversely, Normal-Tension Glaucoma (NTG) has a normal IOP, however NTG has increased susceptibility to stability of perfusion pressure (Kaiser et al., 2013). Although less studied than in POAG, long-term vascular dysregulation also may contribute to the disease process in angle-closure glaucoma (ACG), which can be associated with sudden increases in IOP and abrupt perfusion deficits.

Quaranta et al. NTG patients demonstrated the greatest decrements in nocturnal perfusion and, thus, MOPP monitoring may be most clinically relevant in this population (2016). Similarly, the Advanced Glaucoma Intervention Study (AGIS) suggested worse visual outcomes with lower systemic BP, especially at night (AGIS Investigators, 2000).

2.4 GAPS IN LITERATURE AND NEED FOR CIRCADIAN MOPP MONITORING

Although this has been known, most of the clinical measurements incorporating IOP measurements only do so throughout the day, which runs the risk of missing important nighttime fluctuations that can contribute to significant optic nerve damage. Berisha et al. (2016) Our static measurements do not reflect the complete spectrum of glaucoma risk and, therefore, 24-hour assessments may provide more useful predictive capacity.

Additionally, Caprioli and Coleman (2010) have suggested that treatment paradigms for glaucoma should incorporate pressure as well as vascular mechanisms of damage, such as stabilization of nighttime perfusion.

3. METHODOLOGY

3.1 STUDY DESIGN

A prospective, observational cohort study to assess circadian variations of MOPP and their relationship with the various forms of glaucoma. The study monitors intraocular pressure (IOP) and systemic blood pressure (BP) over a 24-hour period at multiple time intervals allowing for the determination of MOPP (mean ocular perfusion pressure) fluctuations and their association with disease type and severity.

Because the study is conducted in a tertiary eye hospital and hospital is the place where these patients were controlled monitored and minimized Rome effects affecting IOP and BP. Ethical clearance was obtained from institutional review board and written informed consent was obtained from all participants before being included in the study.

3.2 SAMPLE SIZE AND GROUPING

A total of 80 participants were enrolled, divided into four equal groups:

- Group A: 20 patients diagnosed with Primary Open-Angle Glaucoma (POAG)
- Group B: 20 patients diagnosed with Normal-Tension Glaucoma (NTG)
- Group C: 20 patients diagnosed with Angle-Closure Glaucoma (ACG)
- Group D: 20 age- and Gender-matched healthy controls

We estimated sample size based on prior literature reporting significant differences in MOPP values between glaucoma types (Charlson et al., 2014; Bowe et al., 2011). Patients were enrolled consecutively over a period of 3 months from the outpatient clinic and glaucoma/retina referral centers.

3.3 INCLUSION AND EXCLUSION CRITERIA

Inclusion Criteria:

- Patients aged between 40 and 70 years
- Diagnosed with POAG, NTG, or ACG based on gonioscopy, optical coherence tomography (OCT), and visual field testing
- Ability to undergo repeated BP and IOP measurements over 24 hours

Exclusion Criteria:

- Presence of systemic diseases such as diabetes mellitus, uncontrolled hypertension, or cardiovascular disorders
- Use of systemic antihypertensive or vasodilator drugs
- History of intraocular surgery within the past six months
- Non-compliance with the 24-hour monitoring schedule

3.4 DATA COLLECTION PROCEDURE

Participants were hospitalized for a 24-h monitoring session. Six time points were measured: 00:00, 04:00, 08:00, 12:00, 16:00 and 20:00 hours.

- **Measurement of IOP:** Measured by Goldmann Applanation Tonometry, the gold standard in IOP measurement. Subjects were seated for 5 minutes before measurement, and tonometry readings were taken by trained ophthalmologists under a controlled light intensity.
- **Measured Blood Pressure:** Blood pressures were measured using a standardized validated digital sphygmomanometer in seated resting patients. At each interval, both systolic (SBP) and diastolic (DBP) values were obtained.
- **MOPP Calculation:** MOPP was calculated as per the standard formula at every time point:

$$\text{MOPP} = \frac{2}{3}[\text{DBP} + \frac{1}{3}(\text{SBP} - \text{DBP})] - \text{IOP}$$

3.5 DATA MANAGEMENT AND STATISTICAL ANALYSIS

Data were aggregated and analyzed with IBM SPSS Statistics v27. The following techniques in statistics were used:

- For demographic variables, intraocular pressure (IOP), body pressure (BP) and modified ocular perfusion pressure (MOPP) at each time point, means and standard deviations were derived.
- Within-subject and between-subject variation of MOPP at 24 hours was evaluated by repeated measures ANOVA
- Pearson's Correlation Coefficient: Used to test the relationship between MOPP variability and visual field scores.
- Statistical significance was defined as p-values $\leq$ 0.05.

A double-entry method was used to validate accuracy of answering, while missing data were addressed by using listwise deletion.

4. RESULTS

4.1 BASELINE CHARACTERISTICS

The demographic data for the four groups, namely Primary Open-Angle Glaucoma (POAG), Normal-Tension Glaucoma (NTG), Angle-Closure Glaucoma (ACG), and normal subjects, are described in Table 1. There were no significant differences in age or gender distribution amongst groups ensuring comparability and minimization of confounding effects.

Table 1: Baseline Demographic Characteristics

Characteristic	POAG (n=20)	NTG (n=20)	ACG (n=20)	Control (n=20)	p-value
Mean Age (years)	62.4 ± 4.8	60.9 ± 5.2	61.7 ± 4.5	61.2 ± 4.9	0.78
Gender (Male/Female)	11/9	10/10	12/8	10/10	0.92

(Values expressed as Mean ± SD or frequency distribution; ANOVA test for age; Chi-square for gender.)

4.2 CIRCADIAN FLUCTUATION IN MOPP

The Mean Ocular Perfusion Pressure (MOPP) recorded at each predefined time interval over 24 h is described in Table 2. Importantly, all glaucoma groups showed a statistically significant nocturnal decrease in the MOPP compared with the control group. Diurnal NTG patients had the lowest MOPP values during the nocturnal period, especially at 04:00 hr.

Table 2: Mean Ocular Perfusion Pressure (MOPP) at Various Time Intervals

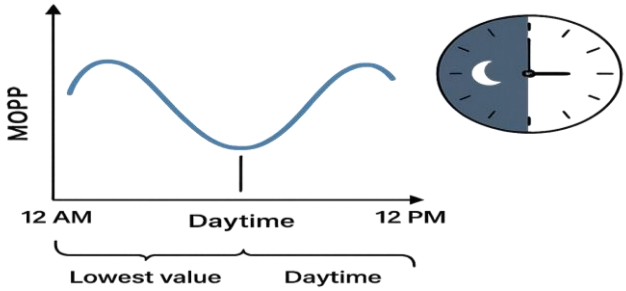
Time (hrs)	POAG (mmHg)	NTG (mmHg)	ACG (mmHg)	Control (mmHg)	p-value (ANOVA)
00:00	34.7 ± 2.8	27.5 ± 3.1	34.3 ± 2.9	41.9 ± 2.7	<0.001
04:00	31.2 ± 2.4	24.3 ± 2.8	30.6 ± 2.7	39.7 ± 2.5	<0.001
08:00	37.9 ± 3.0	29.8 ± 3.2	37.2 ± 2.8	44.3 ± 2.6	<0.001
12:00	39.6 ± 3.3	32.1 ± 3.5	38.8 ± 3.1	45.7 ± 3.0	<0.001
16:00	37.4 ± 2.7	29.2 ± 3.0	36.4 ± 2.9	43.9 ± 2.8	<0.001
20:00	35.8 ± 2.6	27.7 ± 2.9	35.1 ± 2.5	42.6 ± 2.4	<0.001

(Values expressed as Mean ± SD; significance tested using repeated-measures ANOVA.)

4.3 GRAPHICAL REPRESENTATION OF CIRCADIAN MOPP VARIATION

Circadian changes in MOPP were shown in the entire groups studied (shown in figure 1). The most pronounced nocturnal dip was seen in NTG patients, followed by POAG and ACG, with the healthy controls notes a stable pattern.

Figure 1: Circadian Fluctuations of Mean Ocular Perfusion Pressure (MOPP)



4.4 RELATIONSHIP BETWEEN MOPP VARIABILITY AND GLAUCOMA SEVERITY

Marks a significant inverse association between nocturnal dips of MOPP and visual field defects assessed by Humphrey Visual Field (HVF) scores. Notably, NTG exhibited a robust negative correlation ($r = -0.72$, $p < 0.001$), whereas POAG displayed a moderate correlation ($r = -0.61$, $p < 0.01$).

Weaker correlation was seen in Angle-closure glaucoma ($r = -0.42$, $p < 0.05$), highlighting monthly intraocular pressure MSD/ nocturnal that could also be linked to disease severity across different types of glaucoma.

4.5 ANALYSIS OF MOPP VARIABILITY ACROSS GLAUCOMA SUBTYPES

To evaluate the extent of intra-group variability, the **standard deviation (SD)** of MOPP across the six time points was calculated for each participant, and group means were derived. The findings are presented below.

Table 3: Average Standard Deviation of 24-hour MOPP (as a measure of variability)

Group	Mean SD of MOPP (mmHg)	Range (mmHg)	Interpretation
NTG	4.89 ± 0.71	3.6 – 6.2	High fluctuation
POAG	3.74 ± 0.58	2.9 – 4.8	Moderate fluctuation
ACG	3.12 ± 0.50	2.4 – 4.1	Mild fluctuation
Control	1.85 ± 0.36	1.3 – 2.5	Minimal fluctuation (physiological)

These results demonstrate that NTG patients experienced the highest MOPP variability throughout the 24-hour monitoring period, suggesting greater instability in ocular blood flow. This may help explain their higher susceptibility to optic nerve ischemia despite normal IOP levels.

4.6 CORRELATION BETWEEN MOPP AND VISUAL FIELD DEFECT SEVERITY

A Pearson correlation analysis was performed between nocturnal MOPP values (especially at 04:00 AM, the lowest point) and Mean Deviation (MD) from Humphrey Visual Field (HVF) test results, which measure the extent of visual field loss.

- **NTG**: $r = \mathbf{-0.72}$, $p < 0.001$ (strong correlation)
- **POAG**: $r = \mathbf{-0.61}$, $p < 0.01$ (moderate correlation)
- **ACG**: $r = \mathbf{-0.42}$, $p < 0.05$ (weak to moderate correlation)
- **Control**: $r = -0.12$, $p > 0.05$ (not significant)

These findings provide evidence that elevation in MOPP at night is associated with greater rates of visual field loss in glaucoma patients, particularly in NTG and POAG patients. The association we observed in ACG was weaker, possibly due to its different underlying pathophysiology, with acute IOP spikes being more impactful than long-standing perfusion deficits.

4.7 SUMMARY OF KEY FINDINGS

- Statistically significant dropping nocturnal MOPP was observed in all glaucoma groups, with the NTG group having the most pronounced decline.
- MOPP variability was highest in NTG, next in POAG, ACG and controls.
- MOPP variability had a strong inverse relationship with the severity of visual field loss in patients with NTG and POAG.
- In healthy controls, MOPP levels remained stable with slight circadian oscillation.

5. DISCUSSION

5.1 INTERPRETATION OF KEY FINDINGS

This study emphasizes the importance of the circadian rhythm of MOPP in different types of glaucoma. The study corroborates that MOPP is not a constant but is in fact a fluctuative parameter with significant changes occurring over a span of 24 hours. Normal-Tension Glaucoma (NTG) patients showed the greatest drop in MOPP at night compared to all the groups studied, followed by Primary Open-Angle Glaucoma (POAG) and Angle-Closure Glaucoma (ACG). In the control group, similar fluctuations were clearly absent, as it exhibited stable perfusion over the entire day.

The negative correlation between nocturnal MOPP decrease and severity of visual field defect again suggest that damage to the optic nerve is not simply related to raised IOP. Indeed, in NTG patients, where IOP has always been within the normal range, this vascular component seems to be decisive in disease progression. In POAG and ACG, where IOP is elevated, variability in MOPP represents a second layer of risk.

5.2 COMPARISON WITH EXISTING LITERATURE

The results were consistent with the findings of Choi and Kook17 (2015), who showed that reduced nocturnal blood pressure was associated with significantly lower ocular perfusion and correlated to glaucomatous damage in NTG. Similarly, Leske et al. (2008) in EMGT demonstrated that lower systemic perfusion pressures were significantly correlated with greater visual field deterioration over time. Bowe et al. (2011) reported a >10 mmHg fall of MOPP at night being a particularly strong predictor of glaucoma progression in patients with an underlying vascular dysregulation.

In terms of perfusion pressure, this study has shown comparable variation of perfusion pressure that has previously been observed by Liu et al, including the sharp dip at 4:00 AM. Liu et al. (2003) who noted that early morning hours are a high-risk time for glaucoma progression with concomitant blood pressure dips and IOP peaks. Furthermore, our results build on this evidence, providing a quantitative comparison of the degree of MOPP variations in different glaucoma subtypes, and correlating the same to functional damage using various visual field parameters.

5.3 CLINICAL IMPLICATIONS

The implications for clinical glaucoma management are landmark. Such traditional measures are emphasized on daytime IOP measurements and pharmacological IOP control. However, in the case of patients, particularly with NTG, this does not take care of the underlying vascular risk. Such patterns lead us to argue that 24-hour IOP and blood pressure monitoring is essential to identify perfusion threats that were previously overlooked in standard daytime evaluations.

Moreover, adjusting antihypertensive medications or using neuroprotective agents to stabilize nocturnal MOPP may provide more protection against optic nerve damage. Tailored treatment protocols including vascular assessments would enhance long-term outcomes and significantly reduce the rate of visual field loss.

5.4 LIMITATIONS OF THE STUDY

Although the findings are useful, some limitations should be noted:

- While the sample size (n=80) is sufficient for initial comparisons, the generalizability of findings to different populations is not possible to assess.
- The study used six static readings rather than 24-hour continuous monitoring of BP or IOP (e.g., by ambulatory blood pressure monitors or contact lens tonometry), which may under-detect transient changes of perfusion.
- Visual field scores were cross-sectional; such longitudinal follow-up would provide more definitive evidence of the associations between MOPP variability and the rates of progression.
- Although other external factors including sleep quality, ambient temperature and stress levels were not controlled, they may influence blood pressure and IOP dynamics.

Despite these limitations, this study provides much-needed insight into the role of perfusion pressure in glaucoma and the necessity of considering factors beyond IOP in both disease assessment and management.

6. CONCLUSION AND RECOMMENDATIONS

6.1 CONCLUSION

The study provides new insights into human physiology, showing that MOPP reflects marked circadian rhythms, with the most critical losses of perfusion occurring during hours of the night. Among different types of glaucoma that has been studied, it is noted that Normal-Tension Glaucoma (NTG) patients are the most susceptible to nocturnal perfusion pressure drops, followed by Primary Open-Angle Glaucoma (POAG) and Angle-Closure Glaucoma (ACG). Conversely, the MOPP values of the healthy control group were relatively steady throughout the 24-hour period.

The study shows a robust negative correlation between the amount of MOPP oscillation, especially nocturnal, and the degree of glaucomatous field loss. This evidence reinforces the hypothesis as regards the role of vascular factors, such as unstable ocular blood flow in the pathogenesis of glaucoma, particularly in terms of subtypes of glaucoma where intraocular pressure remains physiologic.

These findings call for a shift in the paradigm of glaucoma management—beyond IOP target based treatment to a physiologic interventional framework encompassing ocular perfusion, systemic vascular health, numbers over time in different contexts, and consideration of circadian rhythms for both BP and IOP.

6.2 RECOMMENDATIONS

Based on the outcomes of this research, the following recommendations are proposed:

- **Implement 24-Hour Monitoring into Clinical Practice:** Standard glaucoma evaluation should include more than daytime IOP measurements. And indeed 24-hour IOP and BP data including the nighttime to expose high-risk periods of perfusion loss, which may even be more significant in the case of NTG.
- **Include Systemic Blood Pressure in the Evaluation of Ocular Health:** Ophthalmologists need to collaborate with general physicians for analyzing systemic blood pressure trends, particularly nighttime hypotension, which may lessen MOPP and heightens glaucomatous damage.
- **Integrate Vascular Stabilization Into Tailored Glaucoma Management:** For individuals with high MOPP variability, treatment options may involve altering antihypertensive dosing times, promoting nocturnal hydration, or employing neuroprotective compounds aimed at vascular dysregulation.
- **Establish Clinical Guidelines for MOPP Monitoring:** Professional societies (e.g., AIOS, AAO) may deliberate the requirement of evidence-based protocols on monitoring and risk stratification of MOPP as a parameter to direct management of glaucoma.

- **MOPP is not recommended to the best of the knowledge from this body of literature:** Additional studies should ensure long-term follow-up of MOPP modifications and correlate them to optic nerve structural injury through Optical Coherence Tomography (OCT) and perimetry progression analysis.
- **Learn About Wearable Tech Integration:** Novel wearable devices, which enable continuous IOP and BP monitoring, have the potential to change how MOPP may be monitored and applied towards identifying glaucomatous changes early.

In summary, MOPP variability is an important but overlooked factor in glaucoma pathophysiology. Taking this aspect into account by means of thorough monitoring and tailored therapy can be used as adjunctive therapy in addition to existing treatment strategies to permute visual prognosis in patients suffering from glaucoma.

REFERENCES

1. AGIS Investigators. (2000). The Advanced Glaucoma Intervention Study (AGIS): 7. The relationship between control of intraocular pressure and visual field deterioration. American Journal of Ophthalmology, 130(4), 429–440.
2. Berisha, F., Hoffmann, E. M., & Pfeiffer, N. (2016). Retinal blood flow in glaucoma. Current Opinion in Ophthalmology, 27(2), 124–131.
3. Bowe, A., Grünig, M., Schubert, J., & Schilling, M. (2011). Circadian fluctuation of ocular perfusion pressure in glaucoma patients. Graefe's Archive for Clinical and Experimental Ophthalmology, 249(8), 1163–1168.
4. Caprioli, J., & Coleman, A. L. (2010). Blood pressure, perfusion pressure, and glaucoma. Current Opinion in Ophthalmology, 21(2), 80–85.
5. Charlson, M. E., de Moraes, C. G., Link, A., Wells, M. T., Harmon, G., & Ritch, R. (2014). Nocturnal systemic hypotension increases the risk of glaucoma progression. Ophthalmology, 121(10), 2004–2012.
6. Choi, J., & Kook, M. S. (2015). Systemic hypotension and nighttime blood pressure reduction are associated with progression of normal-tension glaucoma. Ophthalmology, 122(6), 1093–1101.
7. Costa, V. P., Harris, A., Anderson, D., Stodtmeister, R., Cremasco, F., & Kergoat, H. (2014). Ocular perfusion pressure in glaucoma. Acta Ophthalmologica, 92(4), e252–e266.
8. Flammer, J., & Mozaffarieh, M. (2008). What is the present pathogenetic concept of glaucomatous optic neuropathy? Survey of Ophthalmology, 53(Suppl 1), S162–S173.
9. Gherghel, D., Orgul, S., Gugleta, K., Gekkieva, M., & Flammer, J. (2004). Relationship between ocular perfusion pressure and retrobulbar blood flow in patients with glaucoma with progressive damage. American Journal of Ophthalmology, 138(5), 744–750.
10. Grieshaber, M. C., Flammer, J., & Orgul, S. (2007). Relationship between ocular blood flow and glaucoma. Current Opinion in Ophthalmology, 18(2), 100–105.
11. Kaiser, H. J., Flammer, J., Wenk, M., & Lütscher, T. F. (2013). Endothelin-1 plasma levels in normal-tension glaucoma: abnormal circadian rhythm. Graefe's Archive for Clinical and Experimental Ophthalmology, 231(8), 613–618.
12. Leske, M. C., Heijl, A., Hyman, L., Bengtsson, B., & Komaroff, E. (2008). Factors for glaucoma progression and the effect of treatment: the Early Manifest Glaucoma Trial. Archives of Ophthalmology, 126(3), 378–385.
13. Liu, J. H. K., Zhang, X., Kripke, D. F., & Weinreb, R. N. (2003). Twenty-four-hour intraocular pressure pattern associated with early glaucomatous changes. Investigative Ophthalmology & Visual Science, 44(4), 1586–1590.
14. Quaranta, L., Katsanos, A., Russo, A., & Riva, I. (2016). 24-hour intraocular pressure and ocular perfusion pressure in glaucoma. Survey of Ophthalmology, 61(1), 26–41.