DIURNAL VARIATION OF ONSET OF VISUAL LOSS ON PATIENTS DIAGNOSED WITH CENTRAL RETINAL VEIN OCCLUSION

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INTRODUCTION

Central Retinal Vein Occlusion (CRVO) is the second most common retinal vascular disease.[1,2] People over 55 years old are the most common affected. The main risk factors are high blood pressure, dyslipidemia, ocular hypertension, and smoking.[3]

It is believed that CRVO pathophysiology is related to Virchow's triad: endothelial damage, hypercoagulability, and stasis of blood flow, in a site particularly predisposed to thrombosis: the lamina cribrosa.[4]

It is known that human's arterial blood pressure follows a circadian rhythm with a physiologic nocturnal dipping.[5] This nocturnal dipping in blood pressure have been related to some ocular diseases, like non-arteritic anterior ischemic optic neuropathy (NA-AION) and glaucoma progression.[6,7,8]

The hypothesis that NA-AION would be related to a nocturnal event was raised because of the observation that patients predominantly realized the visual loss upon awakening or during the first opportunity to use vision critically. From that observation, Hayreh *et al.* conducted a study to evaluate the time of onset of visual loss in NA-AION and found that 73.3% of patients rnoticed the visual loss in these moments. The authors believe that in a previously affected optic disc, the reduction in its perfusion pressure consequent to the nocturnal dipping in blood pressure, could reach a critical level and lead to optic nerve ischemia.[6,9,10]

The same pathophysiology was suggested to happen in CRVO. However, to the best of our knowledge, studies that verify this relationship between nocturnal blood pressure dipping and CRVO are not available to date.

PURPOSE

To evaluate the time of onset of visual loss in patients with central retinal vein occlusion treated in a tertiary outpatient clinic specialized in retinal diseases in Santo André, Brazil.

METHODS

A cross-sectional study was conducted between July and September 2022. Patients treating for CRVO in a tertiary outpatient clinic specialized in retinal diseases in Santo André, Brazil, were invited to participate in the study. Exclusion criteria were a diagnosis made more than three years before, presence of other retinal diseases, and patients who underwent treatment outside the study institution.

Participants answered to an epidemiologic questionnaire, were interviewed to assess risk factors and were asked to described in detail the moment that they noticed the visual loss. Based on the description, the time of onset of visual loss were categorized in one of the following categories: upon awakening from sleep in the morning, during the first opportunity to use vision critically in the following three hours after awakening, any other time, or could not specify.

Patients' charts were reviewed for assessment of affected eye, time passed since symptoms started, best corrected visual acuity (BCVA), intra ocular pressure (IOP), presence of neovascular glaucoma, retinal neovascularization, cystoid macular edema, and optic disc swelling.

Results were expressed in mean values and standard deviation (SD) for numerical variables and in absolute number and percentage represented for categorical variables. For the statistical analysis, participants who could not specify the time of onset of visual loss were excluded, and participants who noticed the visual loss upon awakening from sleep in the morning or during the first opportunity to use vision critically in the following three hours after awakening were analyzed as a single group as we understand the CRVO probably happened during sleep in both cases.

The G-test were performed to compare the proportions found in our sample and the expected proportions if the time of discovery of visual loss were evenly distributed throughout waken hours, considered to be 16 hours. The software BioEstat® (versão 5.3, Brazil) was used for the analysis and a p-value smaller than 0,05 was considered statistically significant.

RESULTS

26 patients were included in the study, 14 (53,85%) males and 12 (46,15%) females, with a mean (SD) age of 62,96 (11,77) years. The prevalence of main risk factors is described in Table 1.

Table 1. Prevalence of main risk factors for central retinal vein occlusion in the sample studied.

	HPB	Diabetes Mellitus	Dyslipidemia	Smoking	Glaucoma
Total (N=26)	21 (80,77%)	7 (26,92%)	10 (38,46%)	4 (15,38%)	7 (26,92%)

Legend. HPB, high blood pressure.

The mean time between symptom onset and the first retina specialist consultation were 7,31 (7,29) months. Right eye was affected in 10 (38,46%) participants and left eye in 16 (61,54%). The mean (SD) IOP in the affected eye was 17,47 (9,97) mmHg versus 15,13 (3,01) mmHg in the contralateral eye. The further clinical characteristic analyzed are described in Table 2 and the BCVA data described in Table 3.

Table 2. Clinical characteristics of ophthalmological examination.

	NVG	Retinal NV	CME	ODS
Total (N=26)	1 (3.85%)	3 (11,54%)	22 (84,62%)	8 (30,77%)

Legend. NVG, neovascular glaucoma; Retinal NV, retinal neovascularization; CME, cystoid macular edema; ODS, optic disc swelling.

Table 3. Best corrected visual acuity of central retinal vein occlusion patients in the first retinal specialist appointment.

Best Corrected Visual Acuity	≥20/70	<20/70 to 20/200	<20/200 to 20/400	<20/400
Affected Eye (N=26)	3 (11.54%)	7 (26,92%)	1 (3,85%)	15 (57,69%)
Contralateral Eye (N=26)	22 (84,62%)	1 (3,85%)	0	3 (11,54%)

Regarding the time of onset of visual loss, 08 (30,77%) participants could not precisely describe the moment of visual loss and were excluded from this analysis, remaining 18 (69,23%) participants. Out of the participants who were able to describe the moment of visual loss, 07 (38,88%) noticed the visual loss upon awakening in the morning, 05 (27,77%) during the first opportunity to use vision critically in the following three hours after awakening, and 06 (33,33%) in any other time. Together, participants who realized the visual loss upon awakening in the morning or during the first opportunity to use vision critically in the following three hours after awakening accounts for 12 (66,66%) participants. The G-test was performed comparing the proportion found in our sample (66,66%) to the expected proportion if the time of discovery of visual loss were evenly distributed throughout the waken hours (18,75%), being found a statistically significant difference (p<0,0001).

DISCUSSION

This study was conducted to evaluate the diurnal variation of onset of visual loss on patients diagnosed with CRVO because of the hypothesis that these patients predominantly notice the visual loss upon wakening or during the first opportunity to use vision critically early in the day. We found that in our sample, 66,66% of participants with CRVO noticed the visual loss upon awakening from sleep in the morning or during the first opportunity to use vision critically in the following three hours after awakening, being the expected proportion 18,75% if the time of discovery of visual loss were evenly distributed throughout the waken hours, a difference that was statistically significant (p<0,0001).

Although it might seem contradictory at a first look that nocturnal hypotension is related to diseases that high blood pressure is a well stablished risk factor, we believe that the nocturnal blood pressure dipping and consequent decrease in eyes' blood flow might be the trigger to the thrombosis of a central retinal vein that was previously damaged by the well know risk factors; or it might be the final factor to a complete thrombosis of a partially occluded vein that had no clinical repercussion yet.

Discussing our study limitations, our sample size was relatively small considering the prevalence of CRVO, and the study variable was reported by participants, which can be inaccurate and biased. Nevertheless, participants were all being treated in a Brazilian public health care system clinic, which can delay patient access to the retina specialist and contribute to information inaccuracy.

CONCLUSION

To conclude, patients with CRVO predominantly realize the visual loss upon awakening from sleep in the morning or during the first opportunity to use vision critically. This data suggests that CRVO mainly occurs during sleep and therefore that some nocturnal event might act as a trigger for this retinal disease in a patient previously at increased risk.

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