

Co-relation of spontaneous venous pulsations and ocular perfusion pressure in subjects with primary open angle glaucoma (POAG), normal tension glaucoma (NTG) and ocular hypertension (OHT) as compared to controls

Sulatha V. Bhandary^{1,*}, Lavanya G. Rao², Krishna Rao A³, Sindhura Devi Adsumilli⁴, Akshay Sehgal⁵

¹Additional Professor, ^{2,3}Professor & HOD, ^{3,4}Junior Resident, Dept. of Ophthalmology, Kasturba Medical College, Manipal, Karnataka

***Corresponding Author:**

Email: sulatha_bhandary@yahoo.co.in

Abstract

Introduction: Alteration in ocular perfusion pressure and increased venous resistance are known to be associated with glaucoma. Examination of spontaneous venous pulsations can be a surrogate method for assessing the circulation status of optic nerve head and retina. This study is aimed at assessing the prevalence of the spontaneous venous pulsation (SVP) over the optic disc in patients with open angle glaucoma and its co relation to ocular perfusion pressure.

Aim: To analyze the co relation between the presence of spontaneous venous pulsations and ocular perfusion pressure in POAG, NTG, OHT and controls

Materials and Methods: This cross sectional, prospective study. Study period was conducted from September 2013 to June 2015. The study included 334 eyes of 167 patients, (52 patients POAG, 35 each in NTG, OHT and 45 in control group). Spontaneous venous pulsations (SVP) were observed on dilated fundus examination using slit lamp bio microscopy (frequency observed for 20sec) by two ophthalmologists who confirmed each other's findings. Blood pressure was measured in all these patients and ocular perfusion pressure was analysed.

Statistical analysis: Data was analysed using SPSS 16.0 software. Univariate analysis was done.

Results: SVP was absent in 64.4% of POAG (P<0.001) 15.7% of NTG (P=0.871), 10.3% of OHT (P=0.252) and 16.67% of controls. Correlation of mean ocular perfusion pressure and absence of SVP did not show any statistically significant association. Systolic perfusion pressure showed statistically significant co relation to absence of SVP in NTG (p=0.002), OHT (p=0.03). Diastolic Perfusion pressure and absence of SVP was significant in OHT group (p=0.03).

Conclusions: Spontaneous Venous Pulsation has a predictive value as a surrogate method of assessing ocular blood flow, probably an indicator of vascular resistance in the pathogenesis of open angle glaucoma.

Keywords: Blood pressure, Open angle glaucoma, Spontaneous venous pulsations.

Introduction

Spontaneous venous pulsation (SVP) is seen as rhythmic variation in the diameter of the vein on the optic nerve head. It is reported in approximately 80% to 90% of healthy individuals.⁽¹⁾ Studies have shown that SVP is significantly less common in patients with glaucoma than in glaucoma suspects.^(1,2,3) Studies also suggest that glaucoma progression is seen in patients with increased venous pulse pressure.⁽⁴⁾ However role of SVP in glaucoma still remains controversial. To the knowledge of the author, not many Indian studies have assessed the co relation of SVP and Ocular perfusion pressure in glaucoma patients. The current study mainly aims at observing the SVP in Indian patients with POAG, OHT and NTG when compared to the normal subjects and its co relation to ocular perfusion pressure.

Materials and Method

The current cross sectional study was conducted in the Department of Ophthalmology in a tertiary care Centre during the period of September 2013 to June 2015. The patients attending the Ophthalmology department who met the diagnostic criteria of POAG, NTG and OHT were included in the study. Anticipating that the occurrence of glaucoma among the study

population to be 4% and with a 95% confidence level, the minimum sample size of 128 subjects (32 subjects in each group- POAG, NTG, OHT and controls) was chosen. The study included 334 eyes of 167 patients, of whom 52 patients (104 eyes) belonged to POAG, 35 each in NTG, OHT (70 eyes in each group) and 45 patients in control group (90 eyes).

Inclusion criteria: Patients visiting the ophthalmology department of a tertiary care centre who were above the age of 40 years and were diagnosed to have POAG, NTG and OHT following a detailed ophthalmologic evaluation were included.

- POAG (IOP>21mm of Hg with glaucomatous disc and field changes)
- NTG (IOP<21mm of Hg with glaucomatous disc and field changes)
- OHT (IOP>21mm of Hg with normal disc and field)

Exclusion criteria

- History of ocular surgery other than uncomplicated cataract surgery
- History of ocular trauma, uveitis, secondary glaucoma etc.
- Other causes affecting visual fields and patients not willing to give consent.

Age matched controls were selected who came to the department with complaints such as difficulty in reading or dry eye etc.

Ethical clearance was obtained from institutional Ethics Committee.

Spontaneous venous pulsations were observed on dilated fundus examination using slit lamp bio microscopy (frequency observed for 20 seconds) by two ophthalmologists to confirm the finding. Intraocular pressure (IOP) was measured using Goldman Applanation Tonometer, detailed anterior segment and fundus evaluation by slit lamp bio microscopy was done in all selected subjects. The blood pressure was measured in all individuals between 9 am to 11 am and the SPP, DPP, MOPP, MAP were calculated as follows: Systolic perfusion pressure (SPP) = SBP - IOP (Systolic blood pressure - intraocular pressure)
Diastolic perfusion pressure (DPP) = DBP - IOP (Diastolic blood pressure - intraocular pressure) Mean ocular perfusion pressure = (2/3) (MAP - IOP) ((2/3) (Mean arterial pressure - intraocular pressure)).
Mean arterial blood pressure (MAP) = DBP + (1/3) (SBP - DBP).

The data was coded and entered into Microsoft excel spreadsheet and was analyzed using SPSS 16.0 software. Univariate analysis was done and a probability value ('p' value) of < 0.05 was considered as statistically significant.

Results

The study included a total number 334 eyes of 167 patients of whom 52 patients (104 eyes) belonged to

POAG group, 35 each to NTG and OHT (70 eyes in each group) and 45 patients to control group (90 eyes).

The mean age of the patients was 64.29 years in POAG, 63.81 in NTG, 60.69 in OHT and 60.7 years in the controls. Analysis of the gender distribution showed that males were more than the females in POAG and NTG group (63.5% and 62.9%) while females were more in OHT (54.3%)

Frequency of occurrence of spontaneous venous pulsation in the study group showed that SVP was absent in 64.43% of the POAG patients while only 15.7% of NTG and 10.3% of OHT had absent SVP. (Table 1)

Univariate analysis of occurrence of spontaneous venous pulsations in open angle glaucoma when compared to controls showed the following results:

In the POAG group there was a statistically significant association with the absence of SVP (p=0.0001) while the NTG and OHT group did not show statistically significant association. (Table 2)

Co-relation of systolic perfusion pressure, diastolic perfusion pressure and mean ocular perfusion pressure to the absence of SVP showed the following:

The NTG and OHT groups showed a statistically significant association (p=0.002 and 0.03 respectively) between SPP and absence of SVP. However there was no such co relation seen in the POAG group. (Table 3).

The OHT group showed a statistically significant association (p=0.03) between diastolic perfusion pressure and absence of SVP but not in POAG or NTG group. (Table 4).

There was no statistically significant association between absence of SVP and Mean ocular perfusion pressure in any of these three groups: POAG (p=0.361), NTG (p=0.383), OHT (p=0.455). (Table 5)

Table 1: Distribution spontaneous venous pulsations in all the four groups

SVP	POAG n=104	NTG n=70	OHT n=70	Controls n=90
Present	35.57% (37/104)	84.28% (59/70)	89.7% (61/70)	83.33% (75/90)
Absent	64.43% (67/104)	15.72% (11/70)	10.3% (9/70)	16.67% (15/90)

Table 2: Univariate analysis showing the co-relation of SVP in POAG, NTG and OHT with the controls

SVP	POAG		NTG		OHT		Controls	
	N=	%	N=	%	N=	%	N=	%
Present	37	35.57	59	84.28	61	89.7	75	83.33
Absent	67	64.43	11	15.72	7	10.3	15	16.67
P value	<0.0001		0.871		0.252			

Table 3: Comparison of absence of SVP and Systolic perfusion pressure (SPP) in four groups

SPP	OAG n=104	NTG n=70	OHT n=70	Controls n=90
90-110	65.7% n=44/67	9.3% n=4/43	10.6% n=5/47	10.3% n=7/68
110-130	69.2% n=9/13	42.9% n=6/14	0 n=0/7	33.3% n=3/9

>130	58.3% n=14/24 p=0.277	0% n=0/13 p=0.002	37.5% n=6/16 p=0.032	18.2% n=2/13
------	-----------------------------	-------------------------	----------------------------	-----------------

Table 4: Comparison of absence of SVP & DPP (diastolic perfusion pressure) in four groups

DPP	OAG n=104	NTG n=70	OHT n=70	Controls n=90
<60	64.9% n=24/37	23.1% n=4/13	14.7% n=5/34	14.3% n=2/14
60-90	63.6% n=42/66	12.3% n=7/57	17.1% N=6/35	13.5% N=10/76
>90	100% n=1 (p=0.080)	----- (p=0.540)	0% n=0/1 (p=0.032)	-----

Table 5: Comparison of absence of SVP and Mean Ocular Perfusion Pressure (MOPP) in four groups

MOPP	OAG n=104	NTG n=70	OHT n=70	Controls n=90
30-40	64.5% n=20/31	0% n=0/3	16.7% n=3/18	0% n=0/11
40-50	72.0% n=36/50	20.5% n=9/44	11.8% n=4/34	13.6% n=8/59
50-60	47.60% n=10/21	6.7% n=1/15	25% n=4/16	12.5% n=2/16
>60	100% n=1 (p=0.36)	0% n=0/8 (p=0.38)	0% n=0/2 (p=0.45)	50 n=2/4

Discussion

Although the actual mechanism of absence of SVP and its role in glaucoma is still controversial, there are reports suggesting the association of glaucoma with increased retro-laminar venous resistance.⁽⁵⁾ Increased venous resistance could reduce ocular blood flow, thus examination of the SVP may be a surrogate method for evaluating the status of the optic nerve and retinal circulation.^(1,6,7)

The present study included 334 eyes of 167 patients, of whom 52 patients had POAG, 35 each had NTG, OHT and 45 subjects were in the Control group.

Out of the 167 patients, 54.6% were males. The mean age was 60.51 years among the four groups. Almost similar age and gender ratio was noted in other studies by Leske et al, Luciano Bonomi et al, and Ying Feng Zheng et al.^(8,9,10)

Morgan et al reported that SVP was absent in 46% of patients with glaucoma and in 25% of glaucoma suspects.⁽¹¹⁾ Similarly Legler et al found absent SVP in 35.9% of glaucoma patients as compared to 24.7% of suspects.⁽¹²⁾ Balaratnasingam et al also reported that the absence of SVP was a risk factor for glaucoma progression.⁽¹³⁾

Kim et al studied the association of absence of SVP and optic disc hemorrhage. They reported that SVP was absent in 40.3% of the glaucoma patients but there was no co relation between the absence of SVP and the occurrence of disc hemorrhage.⁽¹⁴⁾ Seo et al in another

study showed that spontaneous venous pulsations were absent in glaucoma patients especially in the lower teens (<15 mm of Hg) of intraocular pressure.⁽¹⁵⁾

The present study showed that the absence of spontaneous venous pulsation was higher in Primary Open Angle Glaucoma (64.43%) as compared to controls (16.67%) and the association was found to be significant ($p < 0.0001$). This indicates a decreased optic nerve head perfusion resulting in progressive optic nerve damage in POAG as compared to controls. However, the absence of spontaneous venous pulsations in Normal Tension Glaucoma was 15.72%, ($p = 0.871$), in Ocular Hypertension was 10.3 %, ($p = 0.252$) as compared to Controls (16.67%) and the association was not significant.

Luis A Pinto, et al had studied the absence of spontaneous venous pulsation (SVP) as a vascular risk factor for primary open-angle glaucoma (POAG) using colour Doppler imaging (CDI) and concluded that Glaucoma patients had decreased CRV velocities and also found that SVP was less prevalent in glaucoma patients (50% in POAG, 51% in NTG as compared to 82% in healthy controls).⁽³⁾

In the current study, the blood pressure of the cases and controls was measured and the systolic perfusion pressure, diastolic perfusion pressure and ocular perfusion pressure were co related to the absence of SVP. There was a significant association between systolic perfusion pressure and spontaneous venous pulsations in

NTG ($p=0.002$), OHT ($p=0.032$) as compared to controls while we could not establish a significant association between POAG as compared to controls ($p=0.277$).

Leske et al had studied various risk factors of open angle glaucoma in African population and found that for every 10mm of Hg increase in SPP the relative risk of glaucoma decreased by 0.87 times.⁽²⁾ Luciano Bonomi et al and Ying Feng Zheng did not find demonstrable correlation between systolic perfusion pressure and prevalence of POAG, NTG.^(9,10)

Present study also found a significant association between diastolic perfusion pressure and spontaneous venous pulsations in OHT ($p=0.032$) as compared to controls. However the association was not found to be significant in POAG ($p=0.08$) and NTG ($p=0.540$) as compared to Controls.

Leske et al in their study of open angle glaucoma in African population found that diastolic perfusion pressure of less than 53 mm of Hg was associated with 2.2 times increased risk of developing OAG.⁽⁸⁾ Luciano Bonomi et al found a significant correlation between lower diastolic perfusion pressure and primary open angle glaucoma but there was no significant correlation between low diastolic perfusion pressure and normal tension glaucoma.⁽⁹⁾

Ying feng Zheng et al found that, for every 10mm of Hg decrease in diastolic blood pressure and diastolic perfusion pressure the relative risk of OAG increased by 1.22 times.⁽¹⁰⁾

In this study, the results of comparison of mean ocular perfusion pressure and absence of SVP showed no statistically significant association in any of the three groups. Similarly, Luciano Bonomi et al found no significant correlation between the mean ocular perfusion pressure and POAG.⁽⁹⁾

However, in contrast, Leske et al found that mean ocular perfusion pressure below 40 mm of Hg was associated with 2.6 times increased risk of open angle glaucoma.⁽⁸⁾ Ying Feng Zheng et al also found that lower MOPP was associated with 1.73 times increased risk of open angle glaucoma.⁽¹⁰⁾

Repeated assessment of SVP over the period of observation of patients for glaucoma progression as compared to single assessment, might throw more light on the research question.

Conclusion

To summarise, the present study showed variable association of SVP as a surrogate indicator of vascular resistance. Observation of SVP, being a simple test can only compliment other tests in predicting the prognosis of primary open angle glaucoma.

References

1. Moret F, Polochek CM, Lagreze WA, Bach M, "Visualization of Fundus Vessel Pulsation Using Principal Component Analysis" *Investigative Ophthalmology & Visual Science* (2011)52, 5457-64.

2. Leske MC, Heijl A, Hussein M, Bengtsson B, Hyman L, Komaroff , Early Manifest Glaucoma Trial Group " Factors for glaucoma progression and the effect of treatment: the early manifest glaucoma trial" *Arch Ophthalmol* (2003)121, 48-56.
3. Pinto AL, Vandewalle E, De Clerck E, Marques-Neves C, Stalmans I, " Lack of spontaneous venous pulsation: possible risk indicator in normal tension glaucoma?" *Acta Ophthalmol* (2013)91,514-20.
4. Krakau CE, "Disk hemorrhages and retinal vein occlusions in glaucoma" *Surv Ophthalmol* (1994)38, S18-21.
5. Hayreh SS, Zimmerman MB, Beri M, Podhajsky P, " Intraocular pressure abnormalities associated with central and hemicentral retinal vein occlusion" *Ophthalmology* (2004) 111,133-41.
6. Luo X, Shen YM, Jiang MN,Lou XF, Shen Y, " Ocular Blood Flow Autoregulation Mechanisms and Methods." *Journal of Ophthalmology* (2015) <http://dx.doi.org/10.1155/2015/864871>.
7. Moore D, Harris A, WuDunn D, Kheradiya N, Siesky B, " Dysfunctional regulation of ocular blood flow: A risk factor for glaucoma?" *Clin Ophthalmol* (2008) 2,849–61.
8. Leske MC, Wu SY, Hennis A, Honkanen R, Nemesure B, "Risk factors for incident open-angle glaucoma: the Barbados Eye Studies." *Ophthalmology* (2008), 85-93.
9. Bonomi L, Marchini G, Marraffa M, Bernardi P, Morbio R, Varotto A, " Vascular risk factors for primary open angle glaucoma: the Egna-Neumarkt Study" *Ophthalmology*(2000)107,1287-93.
10. Zheng Y, Wong TY, Mitchell P, Friedman DS, He M, Aung T, "Distribution of ocular perfusion pressure and its relationship with open-angle glaucoma: the singaporemalay eye study" *Invest Ophthalmol Vis Sci.* (2010)51, 3399-404.
11. Morgan WH, Hazelton ML, Cringle SJ, "Retinal venous pulsations in glaucoma and glaucoma suspects". *Ophthalmology* (2004)111, 1489-94.
12. Legler U, Jonas JB, "Frequency of spontaneous pulsations of the central retinal vein in glaucoma" *J Glaucoma.* (2009) 18,210–212.
13. Balaratnasingam C, Morgan WH, Hazelton ML, House PH, Barry CJ, Chan H, Cringle SJ, Yu DY, "Value of retinal vein pulsation characteristics in predicting increased optic disc excavation". *Br J Ophthalmol* (2007) 91,441–4.
14. Kim M, Kim TW, Weinreb RN, Lee EJ, Seo H, "Spontaneous Retinal Venous Pulsation and Disc Hemorrhage in Open-Angle Glaucoma" *Investigative Ophthalmology & Visual Science* (2014)55, 2822-26.
15. Seo JH1, Kim TW, Weinreb RN, Kim YA, Kim M, "Relationship of intraocular pressure and frequency of spontaneous retinal venous pulsation in primary open-angle glaucoma" *Ophthalmology*(2012)119,2254-60.