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Pulsatile Ocular Blood Flow in Healthy Koreans

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***Purpose*:** To determine the normal reference range of pulsatile ocular blood flow (POBF) values in healthy Korean subjects and to find out the factors that may affect them.
***Methods*:** A total of 280 eyes of 280 normal subjects were included in this study. Best corrected visual acuity (BCVA), intraocular pressure (IOP), axial length, POBF, systemic blood pressure, and pulse rate were measured. The mean, standard deviation, range, and the 5th and 95th percentiles of POBF were calculated, and the influences of various parameters to POBF were determined by multiple regression analyses.
***Results*:** The mean POBF value was 766.0±221.6 µl/min in men and 1021.1±249.5 µl/min in women. The 5th and 95th percentiles for POBF values were 486.0 µl/min and 1140.0 µl/min in men and 672.0 µl/min and 1458.0 µl/min in women. The POBF values were significantly influenced by gender, mean blood pressure, pulse rate, and axial length.
***Conclusions*:** Even though the POBF values were influenced by gender, BP, and axial length, we could define the normal reference range of POBF in healthy Koreans.
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Key Words: Korean, Normal reference range, Pulsatile ocular blood flow

Glaucoma is defined as the slowly progressive loss of ganglion cells and their axons in the optic nerve resulting in constriction of visual field. It has been believed that both mechanical and vascular factors are involved in the pathogenesis of glaucoma. Elevated intraocular pressure (IOP) leads to the distortion of optic nerve head, the disruption of axonal transport, and ultimately the deaths of retinal ganglion cells (RGCs). In similar fashion, the RGCs are damaged when the ocular perfusion is interrupted. Many studies have demonstrated that the vascular factors interfere with ocular perfusion and also mediate RGC death. Therefore, many ophthalmologists are concerned about the ocular blood flow and wish to find the methods to measure the ocular blood flow.

For several decades, various techniques have been suggested to evaluate the ocular blood flow, such as pulsatile ocular blood flow (POBF) tonometer, laser interferometry, angiography, laser Doppler flowmetry, and Heidelberg retina flowmeter. Among them, POBF is an ocular hemodynamic parameter that theoretically reflects the pulsatile component of arterial inflow of blood to the intraocular structures. POBF values are derived mathematically by estimating ocular pulse volume changes from continuous pneumotonometric recordings of the ocular pulse pressure wave with computerized tonograph system.[1,2] This system is very easy to perform in clinics and the reproducibility is acceptable.[2,3]

Although numerous preliminary studies suggest that POBF may be a useful assessment of ocular blood flow,[4,5] the reference range of normal POBF values and affecting factors have been established mostly in Caucasians. In current study we examined the reference values of POBF in healthy Korean eyes and found out the factors that affect the POBF using multiple regression analysis.

Materials and Methods

After the approval of the Institutional Review Board, 280 healthy subjects (126 men and 154 women) were recruited for this study. Informed consent was obtained from each participant. All subjects received a full ophthalmic and systemic assessement to exclude those with a history of

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ocular disease, cardiovascular disease, diabetes mellitus, or refractive error of more than 4 diopters. Systemic blood pressure (BP) and pulse rate (PR) were measured using automatic manometer after resting in the sitting position for 15 minutes. Mean BP was calculated as diastolic BP +1/3 (systolic BP-diastolic BP). Axial length was measured with A-scan ultrasonography (Humphrey 820, Allergan Humphrey, US) and IOP was measured with Goldmann applanation tonometer. POBF (µl/min) was measured with POBF tonometer (OBF Labs Ltd, UK) by the same examiner (S.K.K). POBF measurement was conducted in the sitting position with the pneumotonometer probe mounted in a slit lamp microscope, following the instillation of a topical anesthetic (proparacaine 0.5%).

Difference between men and women in age, IOP, mean BP, PR, axial length and POBF were tested for statistical significance by using single factor ANOVA. The mean, standard deviation, range and 5^{th} and 95^{th} percentile values of POBF were calculated separately for men and women. Multiple stepwise linear regression analysis was performed to determine influence of age, IOP, PR, mean BP, and axial length for each gender.

Results

Patient demographics and IOP, PR, BP, and axial length data are shown in Table 1. The age and IOP were not significantly different between men and women. PR and diastolic BP were greater in women (both $p<0.001$), and systolic and mean BP were higher in men than women (both $p<0.001$). Additionally, the axial length was longer in men ($p<0.001$).

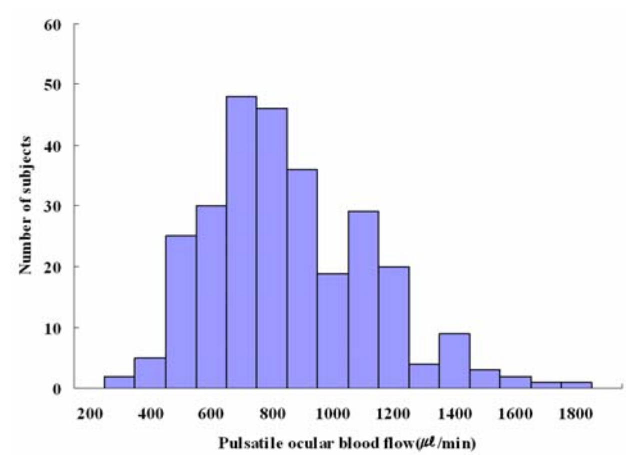

Fig. 1. Distribution of pulsatile ocular blood flow values in healthy Koreans.

Values of POBF are tabled at Table 2. The mean POBF was 766.0±221.6 µl/min for men and 1021.1±249.5 µ1/min for women. Women showed statistically higher POBF values than men ($p<0.001$). The 5^{th} and 95^{th} percentiles for POBF values were 486.0 µl/min and 1140.0 µl/min in men and 672.0 µl/min and 1458.0 µl/min in women. And there was no statistically significant difference in POBF between right and left eyes ($p=0.947$). The distribution of POBF for each gender is shown in Figure 1.

Multiple backward regression analyses were performed. POBF was significantly influenced by axial length (b=-98.798, $p<0.001$), PR (b=5.496, $p<0.001$), and mean BP (b=-6.998,

Table 1. Demographics and intraocular pressure, pulse rate, blood pressure, and axial length data in healthy Koreans

	Male (n=154)	Female (n=126)	*P*-value
Age (years)	42.9±10.4	42.0±9.4	0.381
IOP (mmHg)	14.3±3.0	14.1±3.1	0.591
Axial length (mm)	23.8±0.9	23.1±0.9	<0.001*
PR (beats/min)	72.1±10.0	78.7±12.1	<0.001*
Systolic BP (mmHg)	128.5±13.0	120.0±15.5	<0.001*
Diastolic BP (mmHg)	72.7±8.1	78.4±7.1	<0.001*
Mean BP (mmHg)	97.0±10.1	89.1±11.0	<0.001*

BP=blood pressure; IOP=intraocular pressure; PR=pulse rate; Values given as mean±standard deviation; * $p<0.05$.

Table 2. Values of pulsatile ocular blood flow in healthy Koreans (µℓ/min)

	Male (n=154)	Female (n=126)	*P*-value
Mean POBF	766.0±221.6	1021.1±249.5	<0.001*
Minimun	336.0	540.0	-
Maximum	1788.0	1848.0	-
5^{th} percentile	486.0	672.0	-
95^{th} percentile	1140.0	1458.0	-

Values given as mean±standard deviation; * $p<0.05$.

$p<0.001$), but not age (b=-0.251, $p=0.873$) or IOP (b=-4.144, $p=0.377$). So the regression equation was POBF=3461.944-98.517 x (axial length) + 5.492 x (PR) - 7.149 x (mean BP) (adjusted $R^2=0.241$, $p<0.001$). If the equation of POBF was constructed by each gender, POBF=2698.753-62.354 x (axial length)+2.612 x (PR) - 6.542 x (mean BP) (adjusted $R^2=0.099$, $p=0.001$) for men; and POBF=2914.646-81.985 x (axial length)+3.351 x (PR) - 2.946 x (mean BP) (adjusted $R^2=0.072$, $p=0.003$) for female.

Discussion

Currently, decrease in optic nerve blood flow is understood as the important pathogenesis in glaucoma. There have been various techniques suggested to study ocular blood flow such as laser Doppler velocimetry or fluorescein angiography for the retinal circulation,[6-8] laser Doppler flowmetry for the optic nerve head circulation,[9,10] and color Doppler imaging for the flow in ciliary and orbital vessels.[11,12] But these methods are not easy to be performed routinely in the clinic. POBF tonometry shows more of choroidal vessel, which consists most of the ocular blood flow than the optic nerve head blood flow. However, since all the optic nerve head or choroidal vessel system originates from the posterior ciliary artery and choroidal vessel system always maintains the fixed blood flow because it has no autoregulatory function, we carefully relate the POBF with the ocular blood flow. This system has been developed and measurements are easily and quickly performed and the reproducibility is known to be acceptable.[2,3]

In this study, we studied the normal average of POBF and its relationship with age, sex, IOP, mean BP, PR, and axial length. The 5th and 95th percentiles for POBF values were 486.0 µl/min and 1140.0 µl/min in men and 672.0 µl/min and 1458.0 µl/min in women. Normal reference range of POBF was wide with severe individual variations. The mean POBF value was 766.0±221.6 µl/min in men and 1021.1±249.5 µl/min in women and there was a statistically significant difference between men and women. These values were slightly higher than those of other studies.[2,3,13] We interpreted that the race is one of possible variables.

In this study, POBF was not influenced by age as shown in the previous reports.[2,3,13] This indicates a different result than those reports which show that retinal blood flow decreases due to arteriosclerosis as one ages.[14,15] This discrepancy may be due to increase in ocular rigidity with age.[16,17] Because mathematically derived POBF values require the volume/pressure relationship or ocular rigidity of the eye to conform with the predetermined standard used in the derivation of POBF, a higher POBF value may be obtained if there is an increase in ocular rigidity. The fact that the amount of POBF increases as the scleral rigidity grows due to aging, which countervails the loss from the rise in vascular resistance, can explain the contradicting results.

The influence of PR on POBF was found in this study, and that may account for the difference of POBF between men and women and the wide range and high interindividual variation of normal POBF values. Because POBF represents a fraction of the total cardiac output that is proportional to heart rate and stroke volume, any variation in heart rate should be reflected in the POBF. Therefore it is necessary to ensure that there are no significant differences in heart rate and stroke volume between the two POBF measurements before any changes in the POBF can be attributable to ocular disease, but we did not evaluate the stroke volume in this study. The dependence of POBF on PR has been previously reported with studies using the original Langham OBF system.[3,13,18] In this study only healthy patients with normal BP and IOPs were selected, and no association was found between POBF and systolic BP or IOP. This is in keeping with studies using invasive method of estimating ocular blood flow in animals.[19-22]

POBF decreased as axial length increased in this study. Axial length and POBF statistically shows interesting inverse correlation ($p<0.001$). The women indicate higher POBF than the men. This can be explained by the different axial length, which is the average of 23.8 mm for men and 23.1 mm for women. Normally, as axial length increases, scleral thickness decreases.[23] Therefore, an individual with long aixal length has reduced scleral rigidity and decreased POBF. Several studies reported reduced ocular blood flow in severely myopic patients with increased axial length.[24-29]

In conclusion, POBF shows little difference between Caucasians and Koreans and the normal reference range of POBF is wide with severe individual variations. There are several factors that influence POBF such as sex, PR, mean BP, axial length. Therefore, there will be limits to group examinations or individual comparisons. However, since the POBF measurement using POBF tonometer has a strong reliability as proved in other studies,[2,3] it will be meaningful to observe the continuous change in one subject if variation from the above factors can be controlled or taken into account.

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