Evaluation of Ocular Pulse Amplitude-related Parameters measured by Dynamic Contour Tonometry and Ocular Blood Flow Analyser

Ilsuk Yun, MD, Jaehong Ahn, MD, PhD

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INTRODUCTION

- Normal-tension glaucoma (NTG)
  - Major type of glaucoma in Korea and Japan
- Intraocular pressure & Hemodynamic disturbances(compromised ocular blood flow) is thought to be related to the pathogenesis of NTG
- Pulsatile ocular blood flow (POBF)
  - Related to the pathogenesis of glaucoma
  - Derived from measurement of cyclic change of IOP(OPA)
- Ocular pulse amplitude (OPA)
  - Generated by systemic blood pressure differences during the cardiac cycle
  - Affected by IOP, vascular resistance, choroidal thickness, autoregulation, ocular rigidity
    - Confounding factors generating OPA have been suggested to be related to the pathogenesis of glaucoma
- Ocular rigidity
  - One of the important factors related to the individual susceptibility of the optic nerve head to glaucomatous damage
  - Determined by the pressure/volume relationship within the eyeball

INTRODUCTION

- OPA Estimation
  - By measuring ultra-short-term IOP fluctuations
  - Dynamic contour tonometry (DCT)
    - Can measure OPA by adopting a concave pressure-sensitive tip for continuously measuring transcorneal IOP
  - Ocular blood flow analyzer(BFA)
    - Devices using the pneumatic applanation principle
  - Their measurements could have different relationships with other ocular or systemic hemodynamic parameters due to the use of different measuring algorithms
- In this study
  - Compare OPA measured by both DCT and BFA in terms of their relationship with other ocular and systemic parameters
  - Ocular rigidity-related factor (ORF) was calculated from both DCT and BFA measurements
  - Evaluate ocular pulsatile components and ORF in relation to glaucoma severity in normal tension glaucoma (NTG) patients

MATERIALS AND METHODS

- Cross -sectional and retrospective design
- Subjects
  - who visited the glaucoma clinic at the Department of Ophthalmology of Ajou University Hospital from August 2012 to October 2012 were reviewed
- Exclusions criteria
  - Any history of systemic or ocular disease other than glaucoma
  - Best-corrected visual acuity (BCVA) was lower than 20/30
  - DCT measurements for which the quality score (Q) was > 3
  - BFA measurements that were documented as incomplete or results in tests with high variance comments
  - Unreliable visual field (VF) tests (> 25% fixation loss, false negatives, and false positives)
  - OCT images showing poor centration and signal strength < 7
  - Patients who had previous intraocular surgery, refractive surgery, and laser surgery involving argon laser peripheral iridotomy

Normal (35 eyes)	NTG (42 eyes)
IOP <21 mmHg	Gonioscopically open angle
Normal VF result	at least two reproducible VF test results compatible with glaucoma
No RNFL defect	RNFL defect on OCT, Red-free photographs
No Glaucomatous optic disc	

MATERIALS AND METHOD

Pascal dynamic contour tonometry (DCT)
IOP, OPA

Ocular Blood-Flow analyzer (BFA)
IOP, PA, PV, POBF

Goldman applanation tonometry(GAT)
IOP

Blood pressure

SBP, DBP, MAP(= (SBP+2xDBP)/3), PP, PR

MOPP = 2/3[DBP +1/3(SBP-DBP)] – GAT IOP

ORF = (log IOP1 - log IOP2)/(V1-V2)

CCT, SE

Visual field test (Humphrey field analyzer)

Optical coherence tomography

RESULT

Table 1. Descriptive statistics of enrolled subjects (Mean ± SD)

Parameter	Total (77 eyes)	Normal (35 eye)	NTG (42 eyes)	P value* Normal vs NTG
Age (years)	49.7 ± 11.9	47.0 ± 10.4	51.9 ± 12.7	0.072
Male/female ratio	35/42	17/18	18/24	0.652**
MAP(mmHg)	90.9 ± 11.7	94.2 ± 10.1	88.2 ± 12.4	0.024
PP (mmHg)	48.8 ± 9.3	50.3 ± 10.9	47.5 ± 7.6	0.206
MOPP(mmHg)	45.8 ± 7.6	47.0 ± 6.8	44.8 ± 8.2	0.201
PR	76.1 ± 12.4	77.5 ± 11.5	74.9 ± 13.0	0.359
CCT (μm)	539.60 ± 35.42	545.84 ± 38.06	534.41 ± 32.61	0.160
SE (diopter)	-2.045 ± 2.830	-2.035 ± 2.902	-2.042 ± 2.795	0.996
GAT IOP(mmHg)	14.8 ± 3.0	15.8 ± 3.17	14.1 ± 2.7	0.011
DCT IOP(mmHg)	18.73 ± 3.83	20.03 ± 4.20	17.65 ± 3.16	0.006
OPA (mmHg)	2.69 ± 0.98	2.60 ± 1.05	2.79 ± 0.89	0.376
BFA IOP (mmHg)	21.57 ± 5.30	22.90 ± 5.78	20.47 ± 4.65	0.045
PA (mmHg)	2.99 ± 1.06	3.02 ± 0.90	2.97 ± 1.19	0.852
PV (μl)	5.15 ± 2.00	5.01 ± 1.75	5.29 ± 2.23	0.441
POBF (μl/sec)	12.23 ± 3.98	12.21 ± 3.83	12.25 ± 4.15	0.969
ORF (mmHg/μl)	0.0123 ± 0.0036	0.0126 ± 0.0036	0.0117 ± 0.0027	0.377
MD(dB)	-2.919 ± 6.082	0.352 ± 1.236	-5.649 ± 7.126	< 0.001
PSD(dB)	4.594 ± 4.309	1.751 ± 0.755	6.971 ± 4.610	< 0.001

Table 2. Comparison of IOP differences measured by 3 different devices and correlations between IOP measurements in total patients

Compared Parameters	Mean difference* (± Standard deviation)	P value	Correlation** coefficient between two parameters	P value
GAT IOP – DCT IOP	-3.89 ± 2.32	<0.001	0.796	<0.001
GAT IOP – BFA IOP	-6.73 ± 3.61	<0.001	0.754	<0.001
DCT IOP – BFA IOP	-2.84 ± 3.53	<0.001	0.746	<0.001
OPA - PA	-0.31 ± 0.72	<0.001	0.753	<0.001

SD, Standard deviation; CCT, Central corneal thickness; MAP, mean arterial pressure; PP, pulse pressure; MOPP, mean ocular perfusion pressure; PR, pulse rate; CCT, central corneal thickness; SE, spherical equivalent; GAT, Goldmann applanation tonometry; IOP, intra ocular pressure; DCT, dynamic contour tonometry; OPA, ocular pulse amplitude; BFA, blood flow analyzer; PA, pulse amplitude measured by BFA; PV, pulse volume measured by BFA; POBF, pulsatile ocular blood flow measured by BFA; ORF, Ocular rigidity related factor; MD, mean deviation; PSD, pattern standard deviation; NTG, normal tension glaucoma; *, T-test; **, Fisher's exact test

RESULT

Table 3. Correlations between IOP or OPA-derived parameters and systemic or other ocular parameters in total patients (Pearson correlation coefficient R and P value in parenthesis)

	Age	MAP	PP	MOPP	CCT	SE
GAT IOP	-0.186(0.106)	0.260(0.023)	0.059(0.613)	-0.133(0.249)	0.287(0.011)	-0.272(0.017)
DCT IOP	-0.075(0.516)	0.292(0.010)	0.081(0.485)	-0.018(0.880)	0.229(0.045)	-0.222(0.052)
BFA IOP	-0.141(0.222)	0.311(0.006)	0.112(0.333)	0.018(0.878)	0.138(0.231)	-0.227(0.047)
OPA	0.073(0.529)	-0.019(0.872)	0.109(0.344)	-0.138(0.231)	-0.083(0.474)	0.234(0.041)
PA	0.058(0.614)	-0.029(0.805)	0.097(0.399)	-0.036(0.755)	-0.121(0.296)	0.397(<0.001)
POBF	0.057(0.621)	-0.184(0.109)	-0.017(0.881)	-0.088(0.448)	-0.214(0.062)	0.433(<0.001)
ORF	0.009(0.940)	0.028(0.812)	0.081(0.485)	-0.124(0.283)	0.023(0.840)	-0.211(0.066)

Table 4. Correlations between OPA-derived parameters and IOP measurements in total patients (Pearson correlation coefficient R and P value in parenthesis)

	GAT IOP	DCT IOP	BFA IOP	OPA	PA	POBF
OPA	0.300 (0.008)	0.347 (0.002)	0.268 (0.018)		0.753 (<0.001)	0.512 (<0.001)
PA	0.020 (0.865)	0.045 (0.700)	0.083 (0.472)	0.753 (<0.001)		0.743 (<0.001)
POBF	-0.252 (0.027)	-0.276 (0.015)	-0.366 (0.001)	0.512 (<0.001)	0.743 (<0.001)	
ORF	0.380 (0.001)	0.279 (0.014)	0.504 (<0.001)	0.267 (0.019)	-0.283 (0.013)	-0.398 (<0.001)

IOP, intraocular pressure; GAT, Goldmann applanation tonometry; DCT, dynamic contour tonometry; BFA, blood flow analyser; OPA, ocular pulse amplitude measured by DCT; PA, pulse amplitude measured by BFA; POBF, pulsatile ocular blood flow measured by BFA ; ORF, Ocular rigidity related factor; MAP, mean arterial pressure; PP, pulse pressure; MOPP, mean ocular perfusion pressure; CCT, Central corneal thickness; SE, spherical equivalent

RESULT

Table 5. Correlations between IOP or OPA-derived parameters and indices of glaucomatous damages in normal tension glaucoma patients (Pearson correlation coefficient R and P value in parenthesis)

			RNFL thickness				
	MD	**PSD**	**Temporal**	**Superior**	**Nasal**	**Inferior**	**Average**
GAT IOP	-0.300 (0.054)	0.111 (0.485)	-0.014 (0.928)	-0.099 (0.534)	-0.217 (0.167)	0.004 (0.982)	-0.106 (0.505)
DCT IOP	-0.073 (0.645)	0.012 (0.939)	-0.156 (0.322)	-0.020 (0.898)	-0.101 (0.525)	-0.172 (0.275)	-0.128 (0.418)
BFA IOP	-0.244 (0.120)	0.161 (0.308)	-0.054 (0.733)	0.070 (0.661)	-0.137 (0.387)	-0.276 (0.077)	-0.131 (0.409)
OPA	-0.128 (0.418)	0.192 (0.224)	-0.090 (0.569)	-0.018 (0.911)	0.070 (0.659)	-0.019 (0.904)	-0.010 (0.949)
PA	0.016 (0.921)	0.135 (0.394)	-0.046 (0.771)	0.149 (0.345)	0.196 (0.213)	0.139 (0.381)	0.154 (0.332)
POBF	0.119 (0.454)	0.067 (0.675)	0.068 (0.670)	0.267 (0.087)	0.282 (0.071)	0.316 (0.042)	0.323 (0.037)
ORF	-0.385 (0.012)	0.138 (0.385)	-0.031 (0.845)	-0.250 (0.111)	-0.327 (0.034)	-0.416 (0.006)	-0.351 (0.023)

IOP, intraocular pressure; OPA, ocular pulse amplitude; GAT, Goldmann applanation tonometry; DCT, dynamic contour tonometry; BFA, blood flow analyzer; PA, pulse amplitude measured by BFA; POBF, pulsatile ocular blood flow measured by BFA; ORF, Ocular rigidity related factor; MD, mean deviation; PSD, pattern standard deviation; RNFL, retinal nerve fiber layer.

DISCUSSION

- Compromised ocular blood flow
  - Reported as supporting evidence for a vascular mechanism of glaucoma pathogenesis
  - POBF may be influenced by the presence of glaucoma and IOP level
- Topical IOP-lowering medications in the glaucoma could influence OPA
  - No significant difference in POBF was found between medically treated glaucoma patients and normal subjects
  - Ocular rigidity, OPA, and POBF in treated OAG patients did not differ from those of normal subjects by study using invasive manometric techniques
  - We also found that ocular pulsatile components (including POBF) of NTG patients did not differ significantly from those of normal subjects (Table 1)

DISCUSSION

- Pulsatile ocular blood flow
  - An estimated parameter representing the pulsatile components of ocular blood flow
  - Depends on measurements of ultra-short-term IOP fluctuation(OPA)
    - ⇒ OPA Regarded as surrogate marker of POBF

- In our Study
  - DCT OPA showed a good correlation with BFA PA (Pearson r = 0.753), but its correlation coefficient (r = 0.512) with POBF was lower than that of BFA PA (r = 0.743)(Table 4)

  - DCT OPA correlated significantly with IOP measurements, while BFA PA did not (Table 4).

  - DCT OPA has some limitations as a surrogate for POBF
    - More influenced by IOP level and less strongly associated with POBF than BFA PA

DISCUSSION

- In our study
  - The ORF of NTG patients was not higher than that of normal subjects(Table1)
    - Possible that IOP-lowering therapy may have influenced the results because ORF correlated significantly with IOP level in our study(Table4)
  - Ocular rigidity estimating methods using ocular pulsatile components may have an intrinsic limitation
    - Cannot measure specific responses of important regions related to glaucoma pathogenesis: the lamina cribrosa or peripapillary sclera
- Although the ocular rigidity coefficients differed according to the estimating method, they may represent different aspects of the same ocular property that connects the hemodynamic factors with biomechanical ones in the pathogenesis of glaucoma
- Glaucomatous damage may associated with ocular rigidity
  - Increased : Representing global stiffness of the eyeball, because a higher value indicates greater IOP elevation for a given change in ocular volume.
  - A lower rigidity of a specific region – posterior sclera including the foveal area, may be interpreted as weaker scleral support for the optic nerve axons in the lamina cribrosa

DISCUSSION

- Lower OPA was not associated with more severe glaucomatous damage
  - Neither DCT OPA nor BFA PA showed any significant correlation with parameters representing glaucomatous damage(Table 5)
- Lower POBF was significantly correlated with lower RNFL thickness in treated NTG patients in our study (Table 5)
- POBF and ORF were correlated significantly with some OCT parameters in NTG patients(Table5)
- ORF showed a significant correlation with VF defects (Table 5).
  - ⇒ suggests that lower POBF and higher ocular rigidity may be associated with greater glaucomatous damage in NTG patients
- Conclusion
  - DCT OPA can be used as a surrogate for POBF
    - It showed good correlations with POBF and BFA PA
    - In treated NTG patients – decreased POBF and increased ocular rigidity may be related to the severity of glaucoma