학동기 근시화에 따른 시신경 유두함몰비의 변화

The Change of Cup-to-Disc Ratio during Childhood Myopic Shift

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Purpose: During eyeball growth in children, a progressive disc tilting and the elongation of the eyeball is observed. However, the glaucomatous eyes in childhood are still evaluated mainly with cup-to-disc ratio (CDR). On the basis of this background, the authors aimed to study the impact of elongation of eyeball and progressive disc tilting to CDR in eyes with childhood myopia.

Methods: Total of 68 eyes from 34 subjects younger than 14 years of age were included in the study. Serial disc photographs were reviewed retrospectively. The changes in the ratios of vertical disc diameter, cup-to-disc area, tilt ratio, torsion degree, disc to foveal angle, and peripapillary atrophy (PPA) and the relationships between the degree of axial elongation or the CDR were analyzed. Patients were divided into two groups according to the change of the CDR. When CDR decreased at last follow-up compared to the baseline, they were classified as 'decreased CDR group'.

Results: The only value significantly different between the increased and decreased CDR groups was the change of tilt ratio ($p = 0.009$). Furthermore, in univariate and multivariate regression analysis, the change of CDR was negatively associated with changes of tilt ratio ($p = 0.019$, $r = -0.284$), but the other factors as spherical equivalent (SE), SE change, baseline disc area, torsion degree, disc-foveal angle change, and PPA change were not significantly associated with the change of tilt ratio.

Conclusions: During axial elongation occur in children, in the cases that the tilting is the main change of the optic disc, the CDR may be underestimated, and therefore the physicians should bear in mind that glaucomatous change can be underestimated as well.

Key words: Optic disc, Glaucoma, Myopia

Introduction

Myopia is the main clinical concern of the Asian children in recent years, and the prevalence of which has grown throughout the decades.^{1,2} It is now also well known that myopia is one of important risks of glaucoma,³ especially due to structural changes as a result of the axial elongation. The prevalence of myopia is increased in patients with ocu-

lar hypertension, primary open angle glaucoma, and especially normal tension glaucoma (NTG).⁴⁻⁶

However, changes in the optic disc morphology and peripapillary region occurs in children who undergo axial elongation.⁷⁻¹⁰ In several studies, myopic eyeball growth influenced the disc to enlarge in its area and resulted larger cup-to-disc ratio (CDR).¹⁰⁻¹³ Other than measurement errors in myopic optic disc, changes in the optic disc morphology during axial elongation in childhood may also affect the evaluation of the optic disc during glaucoma examinations. Disc tilting is a known factor to influence the evaluation of CDR, which makes underestimation of the CDR. This disc morphological changes by myopia does not occur uniformly. Our group previously showed that change in the disc morphology during childhood myopic shift were different between normal eyes, disc suspects with enlarged CDR,

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and glaucomatous eyes.¹⁰ All these findings may suggest that there may be factors that should be considered when evaluating the CDR in eyes of children. In this study, we investigated the change of CDR during childhood myopic shift and related factors.

Materials and Methods

Subjects younger than 14 years of age who developed myopia with serial optic disc photographs were included in this study. Subjects were enrolled from a database of patients examined at the pediatric clinic of Seoul St. Mary's Hos-

pital. Medical records of myopia were reviewed between February 2008 and January 2015. The Institutional Review Board of Seoul St. Mary's Hospital approved this study, which adhered to the principles of the Declaration of Helsinki. Written informed consent was obtained from the next of kin, or guardians on behalf of the children.

Each subject received an ophthalmic examination including a medical history review, the measurement of cycloplegic refraction with automated refractometer, slit-lamp biomicroscopy, gonioscopy, axial length measurement using IOL master (Carl Zeiss Meditec, Jena, Germany) and disc photography (Kowa VX-10, Nagoya, Japan). For inclu-

Figure 1. Measurement of disc parameters from disc photograph. Cup-to-disc area ratio (A), cup area (B), tilt ratio (C), and torsion degree (D) were measured from each disc photographs.

sion of the study, subjects had to have at least two optic disc photographs with an interval of at least 6 months.

The disc photographs were taken using a digital camera (Kowa VX-10, Nagoya, Japan) after maximal pupil dilatation. The optic disc images were independently evaluated by two observers (YRP and HYP) who were blinded to each other.

The serial disc photographs were assessed by one observer (YRP) who was not aware of the patients' medical records. The outlines of the optic disc (the inner border of Elschnig's scleral ring) and PPA (an inner crescent of chorioretinal atrophy with visible sclera and choroidal vessels) were depicted using ImageJ software (available at <http://rsb.info.nih.gov/ij/index.html>). The circumference area of the disc, maximum PPA width, tilt ratio, torsion degree were then measured from the baseline and final disc photographs (Fig. 1). The CDR was defined as the inner area of drawn optic disc margin divided by the inner area of cup margin. The PPA width was plotted using a mouse-driven cursor to pursue the optic disc and PPA margins directly onto the image. The tilt ratio was determined by the ovality index (shortest diameter/longest diameter), and the torsion degree was prescribed by the degree between the vertical meridian and the longest diameter of the delineated disc margin.

Patients were divided into two groups according to the change of the CDR that was measured on disc photograph as CDR area ratio. When CDR increased at last follow-up compared to the baseline, they were classified as 'increased CDR group'. When CDR decreased at last follow-up compared to the baseline, they were classified as 'decreased CDR group'.

Statistical Analysis

The intraobserver and interobserver reproducibility of the measurements of the optic disc parameters were evaluated by calculating intraclass correlation coefficients. To evaluate the interobserver reproducibility of our values 20 randomly chosen disc photographs were assessed by two examiners.

The Comparisons between two groups were analyzed with Student's *t*-test or the Mann-Whitney *U*-test. The chi-

square test was used to compare frequencies. To identify the factors associated with the CDR changes, univariate and multivariate logistic regression were conducted. The variables showing significance values of $p < 0.20$ on the univariate analysis were included in the multivariate model. Correlation studies were performed with Pearson's correlation analysis. A *p*-value of less than 0.05 was considered to be statistically significant. Statistical analysis was performed using the SPSS statistical program (IBM Corp., Armonk, NY, USA).

Results

The study comprised 68 Korean pediatrician eyes (28 male; 40 female). Further subject details are given in Table 1. The mean age of the participants was 7.64 ± 2.55 years (range, 2 to 14), the mean axial length and baseline spherical equivalent (SE) were 23.59 ± 1.55 mm (range, 20.19 to 25.49) and 0.53 ± 0.83 Diopter (range, -12.25 to +6.625).

In the Pearson's correlation analysis, there was a decrease in the CDR as greater myopic shift occurred ($r = 0.410$, $p = 0.032$). When the baseline disc area was smaller, the decrease in CDR was greater ($r = 0.507$, $p = 0.039$) (Fig. 2). Among disc morphological parameters, such as change in the disc tilt ratio, disc torsion, disc-foveal angle, and PPA area, increase in the tilt ratio was significantly related to the decrease in CDR ($r = 0.702$, $p < 0.001$). Also, increase in

Table 1. Characteristics of childhood subjects with myopic shift

Characteristics	Value
Number	68
Gender (male:female)	28:40
Age (years)	7.64 ± 2.55
Axial length (mm)	23.59 ± 1.55
Baseline refraction (SE) (diopters)	-0.95 ± 3.82
Baseline vertical CDR	0.53 ± 0.83
Baseline tilt ratio	1.17 ± 0.10
Baseline torsion degree (degree)	13.68 ± 11.98
Baseline PPA area (pixel area)	20.97 ± 10.59

Values are presented as mean $\pm$ SD unless otherwise indicated. SE = spherical equivalent; CDR = cup to disc ratio; PPA = peripapillary atrophy.

Figure 2. Scatterplot of cup-to-disc ratio change according to spherical equivalent (A) and disc area (B).

disc torsion degree was significantly related to the change of CDR ($r = 0.694$, $p < 0.001$) (Fig. 3).

We classified children into two groups according to the change of CDR. There were 34 children with reduced CDR during myopic shift and 34 children with increased CDR during myopic shift. The comparisons between two groups are listed in Table 2. The only significant difference between the two groups was the change of tilt ratio ($p = 0.009$, comparison by Student's t -test). Furthermore, in univariate and multivariate regression analysis, the change of tilt ratio was significantly associated with the changes of CDR ($p = 0.019$, $\beta = -0.284$). Myopic factors, such as baseline spherical equivalent (SE) and SE change, were not related to the change in CDR (Table 3).

Discussion

Myopia is an uprising ocular condition, with prevalence of about 80% in East Asia among younger populations.^{2,14-17} As the axial length grows, the disc becomes more tilted, forming a temporal crescent.^{7,11,18} The progressive alterations in the optic disc and the enlargement of PPA in myopic eyes have been suggested that the changes are due to scleral stretching resulted by the axial elongation of the eyeball,^{7,19} and the optic disc of the myopic patients become more dif-

ficult to assess. There are several studies which suggest that myopic eyes have larger optic disc size,^{4,7,20,21} and increased prevalence of glaucoma.^{3,4,9} Jonas et al. evaluated the optic disc in myopic open angle glaucoma subjects, and claimed that the optic disc was significantly larger and shallower in the myopic eyes,^{9,21} and in a recent study Nagaoka et al. presented that highly myopic individuals showed higher prevalence in glaucoma with larger optic disc size.⁹ Even though disc area is an important value, there are several studies that it is difficult to assess them in eyes with co-existing glaucoma.^{8,12} From the evidences above, the CDR is one of the key factors when clinicians make decisions in cases of glaucoma, but it could be misguided when confounded by myopia.

In this study, we discovered that when an eye elongates in children, the appearance of the disc changes related to the change of disc tilt. As disc tilting occurs, CDR get smaller, which could mean underestimation by fundus examinations. It is worth mentioning that this change is mainly due to the change of the morphology of the optic disc, rather than the change of the refraction itself. The change in CDR was independent of myopic parameters, but only the disc parameters. Our result is consistent with the former studies, that claimed of the positive relationship of the axial length and the tilt ratio.^{18,22-24} Furthermore, the eyes with larger disc sizes and larger baseline CDR went through more

Figure 3. Scatterplot of cup-to-disc ratio change according to disc parameters.

changes. In other words, the eyes with physiologic large cup experienced a bigger alteration in terms of morphology as they grew longer, and the CDR of these eyes could be more underestimated.

There are numerous former studies that claims that myopic eyes tend to have tilted optic disc,^{18,25-27} and some presents that the degree of myopia and the axial elongation of the eye have been correlated with the severity of the tilt ratio.^{18,26} Furthermore, the myopia has been repeatedly mentioned as a confounding factor when making a diagnosis in glaucoma suspect patients,^{28,29} and it is mainly due to morphologic change of the myopic optic disc, including the tilting of the

optic disc. There even have been attempts to surmount such diagnostic challenge.^{22,30,31} Hwang et al tried to investigate the correlation between the optic disc tilt and the peripapillary retinal fiber layer thickness,²² and Kim et al introduced a novel method for screening glaucomatous sign in tilted myopic eyes.³⁰ Shin et al discovered that diagnostic capabilities of the CDR in the tilted disc eyes were inferior to those in the non-tilted disc eyes.³¹ Additionally, our study shows that change of the CDR reduction due to disc tilting occurs in some myopia-developing eyes. As shown in a representative case (Fig. 4), if we met this patients after the development of morphological changes in the optic disc at

Table 2. Comparison between childhood subjects with or without changes in the cup-to-disc ratio

	Reduced cup-to-disc ratio (n = 34)	Increased cup-to-disc ratio (n = 34)	p-value
Age at baseline (years)	8.29 ± 2.79	6.94 ± 2.76	0.049*
Gender (male:female)	15:19	13:21	0.720†
Duration between baseline and final follow-up (years)	3.54 ± 2.96	3.29 ± 2.32	0.310*
Spherical equivalent (diopter)			
Baseline	-1.04 ± 1.65	-0.33 ± 1.74	0.275*
Final	-1.47 ± 3.74	-0.74 ± 3.28	0.417*
Changes	-0.40 ± 3.74	-0.47 ± 2.73	0.910*
Baseline disc area (pixel area)	32,492.80 ± 23,536.24	27,769.54 ± 5,511.21	0.259*
Cup-to-disc ratio			
Baseline	0.55 ± 0.10	0.49 ± 0.05	0.002*
Changes	-0.05 ± 0.06	0.03 ± 0.03	<0.001*
Optic disc morphological changes			
Tilt ratio change	0.07 ± 0.14	-0.00 ± 0.04	0.009*
Torsion degree change (degree)	-1.24 ± 5.68	1.30 ± 5.49	0.078*
Disc-foveal angle change (degree)	0.62 ± 2.81	-0.63 ± 2.55	0.070*
Peripapillary atrophy area change	-3.92 ± 11.12	-2.30 ± 8.38	0.510*

Values are presented as mean ± SD unless otherwise indicated.

*Student's *t*-test; †Chi-square test.

Table 3. Related factors to cup-to-disc ratio changes in childhood subjects with myopic shift

	Univariate analysis			Multivariate analysis		
	Beta	95% CI	p-value	Beta	95% CI	p-value
Age	-0.174	-0.009 to 0.002	0.156	-0.083	-0.008 to 0.004	0.521
Baseline SE	0.039	-0.004 to 0.005	0.752			
SE change	0.030	-0.005 to 0.006	0.868			
Baseline disc area	-0.064	0.000 to 0.000	0.603			
Tilt ratio change	-0.284	-0.297 to -0.028	0.019	-0.260	-0.296 to 0.002	0.042
Torsion degree change	0.200	0.000 to 0.005	0.119	0.128	-0.001 to 0.004	0.320
Disc-foveal angle change	-0.131	-0.009 to 0.003	0.309			
Peripapillary atrophy area change	0.001	-0.002 to 0.002	0.991			
Duration between baseline and final follow-up periods	0.053	-0.080 to 0.062	0.794			

Variables exhibiting significance values of $p < 0.20$ upon univariate analysis were included in the multivariate model. Logistic regression analysis with dependent variable as the presence of optic nerve head/peripapillary atrophy changes.

CI = confidence intervals; SE = spherical equivalent.

adulthood, larger CDR in childhood may have been underestimated.

The limitations of this study were a small number of the subjects, and that it was a retrospective design and the selection bias could not be ruled out. Nevertheless, there were no formal studies, to our knowledge, that exhibited the axial

elongation with optic disc tilting could confound the size of cup to disc ratio and that can be underestimated.

In conclusion, the eyes going through childhood myopic shift should be more carefully evaluated and especially when disc tilting is present. When we encounter these myopic eyes at adulthood, underestimation of the CDR may

Figure 4. Representative case showing cup-to-disc ratio underestimation after disc morphological changes.

mask the evaluation of the glaucoma. Classifying child undergoing myopic shift with or without disc morphological changes may help in the future evaluation of CDR in these patients.

Conflict of Interest

The authors declare that there are no conflict of interests regarding the publication of this paper.

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