• Clinical Research •

Effects of congenital ptosis on the refractive development of eye and vision in children

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Abstract

● **AIM:** To investigate the influence of unilateral congenital ptosis on the development of the eye and vision in children.

● **METHODS:** In this prospective observational study, 41 patients with unilateral congenital ptosis were enrolled (age range 3-15y). The blepharoptosis was divided into 3 subgroups according to the margin reflex distance-1 (MRD-1), including mild group (MRD-1≥2 mm), moderate group (0≤MRD-1<2 mm), and severe group (MRD-1<0 mm). The fellow eyes served as controls. All subjects underwent ocular examinations, including axial length, keratometry, and refractive error.

● **RESULTS:** The incidence of astigmatism (ptotic eyes: 58.5% *vs* fellow eyes: 24.4%, *P*=0.002) and magnitude of cylindrical power (ptotic eyes: -0.86±0.79 D *vs* fellow eyes: -0.43±0.63 D, *P*=0.003) differed significantly between the ptotic eyes and the fellow eyes. The spherical equivalent refraction (*P*=0.006), spherical power (*P*=0.01), cylindrical power (*P*=0.011), axial length-corneal radius (AL/CR) ratio (*P*=0.009), frequency of hyperopia (*P*=0.002) and astigmatism (*P*=0.004) were significantly different among the ptotic eye subgroups and the fellow eye group. In addition, in patients with congenital ptosis, the incidence of amblyopia is 43.9% and the incidence of anisometropia is 24.4%. More importantly, the ratio of AL/CR showed significantly positive correlation with the severity of ptosis (*P*=0.002).

● **CONCLUSION:** Congenital ptosis may lead to a delayed eyeball development in the aspect of AL/CR. The risk of amblyopia is also increased due to visual deprivation and aggravated anisometropia, particularly in severe ptosis case.

● **KEYWORDS:** unilateral congenital ptosis; axial length; AL/CR ratio; amblyopia

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INTRODUCTION

The models of form-deprivation were established by suturing of the eyelids or covering the eyes with occluders which has been reported to induce eye axial length (AL) elongation in the chickens[1], guinea pigs[2], mice[3-4], and primates[5]. Congenital ptosis defined as abnormally low-lying upper eyelid margin in primary gaze is also a representative entity that causes form deprivation[6-7]. The relationship between congenital ptosis and axial elongation remains controversial. Several studies[6,8] reported a higher frequency of axial myopia in eyes with congenital ptosis compared with the normal eye, whereas others indicated congenital ptosis may have little effect on axial globe length elongation[9]. The correlation between AL and corneal curvature radius (CR) was proved to be strong and positive, when it reaches a peak at emmetropia, and is lower for myopes and hyperopes[10]. Compared with the AL alone, the axial length-corneal radius (AL/CR) ratio was then found to be more representative of the refractive state and the shape of the eye[10-15]. Once AL matches CR, emmetropia refraction will be produced and refractions will become myopic as the ratio of AL/CR begins to exceed about 3.0[12]. AL/CR ratios can be a helpful marker of the development of the eyeball. Therefore, this study sought to examine and compare the refractive status, AL/CR ratio and other parameters of eyes in children with unilateral congenital ptosis, and further investigate the effect of the severity of ptosis on the development of eyeball.

SUBJECTS AND METHODS

Ethical Approval All procedures of this study were approved by the Ethical Committee in Tianjin Medical University Eye Hospital and in accordance with the tenets of the Declaration of Helsinki. Institutional Review Board of the Ethics Committee of National Center for Women Children's Health Chinese Center for Disease Control and Prevention, Tianjin, China (No. FY2016-003). Written informed consent forms were obtained from all the participants enrolled in this study after a thorough explanation of the study objective and methods.

Forty-one patients with the diagnosis of congenital ptosis at Tianjin Medical University Eye Hospital (Tianjin, China) between July 2017 and September 2018 were enrolled in the current study. The patients were at 3 to 15 years of age, with unilateral congenital ptosis. Exclusion criteria include: 1) other ophthalmic or systemic disorders (such as corneal opacity, congenital cataract, and strabismus); 2) history of eyelid surgery or use hard contact lens that may cause aponeurotic ptosis and changes of corneal shape. Unilateral congenital ptosis was confirmed in all patients by an experienced ophthalmologist. Blepharoptosis was further divided into 3 subgroups according to the margin reflex distance-1 (MRD-1): mild group (MRD-1≥2 mm), moderate group (0≤MRD-1<2 mm), and severe group (MRD-1<0 mm). The MRD-1 is a measurement from the central upper eyelid margin to the pupillary light reflex in the primary eye position[16]. The fellow eyes served as control group. The ocular biometric parameters (AL and keratometry) was measured using an ocular biometry system (IOL Master; version 5.02, Carl Zeiss Meditec, Oberkochen, Germany). The patients' droopy eyelid was lifted to expose the pupil using gentle finger force to avoid pressure on the eyeball during the measurements. We measured the AL at least three times and considered valid if individual measurements varied by no more than 0.02 mm[14]. Refractive power was measured using a desktop autorefractor (KR-8800; Topcon Corporation, Tokyo, Japan). Cycloplegic refraction was measured after three administrations cyclopentolate hydrochloride eye drops at 10-min intervals. Acuity was examined with refractive correction for those with refractive error and determined using a Snellen chart.

Definitions The AL/CR ratio was defined as the AL divided by the mean CR. The refraction was calculated as SER (spherical degree+0.5×cylinder degree). Myopia was defined as SER greater than or equal to -0.50 D, hyperopia as SER ≥+0.50 D and emmetropic as SER lower than 0.50 D. Astigmatism was defined as ≥0.75 cylinder degree. A difference in SER of 1.00 D or more between the two eyes were recognized as anisometropia[17]. Amblyopia was defined as two Snellen lines or more difference between the two eyes while wearing the proper prescription, or lack of central, steady and maintained fixation in the ptotic eye with presence of normal central, steady and maintained fixation in the nonptotic eye[18].

Statistical Analysis Statistical analyses were performed using Statistical Program for Social Sciences 20.0 (IBM SPSS Inc., New York, NY, USA). All data were expressed as mean±standard error of mean (SEM). The data were examined using the D'Agostino and Pearson omnibus normality test. The data with a Gaussian distribution were further examined by Levene test to confirm homogeneity of variance. The differences among the ptosis subgroups and the healthy controls were then analyzed by one-way ANOVA followed by a Tukey post hoc. For the data with nonparametric distribution, the differences among groups were analyzed by Kruskal-Wallis test followed by Dunn's post hoc. The associations between the parameters were analyzed by Spearman's correlation analysis. A P value less than 0.05 was considered statistically significant.

RESULTS

All data and results are summarized in Tables 1 and 2. Forty-one patients (28 males, 13 females; mean age: 7.78±3.28y; range: 3-15y) were included in this study (Table 1). No significant difference in the incidence of amblyopia (χ^2=2.620, P=0.270) was found among the ptosis patients sub-grouped according to the MRD-1 (Table 1 and Figure 1A). Ten (24.4%) of the 41 patients with congenital unilateral ptosis were diagnosed with anisometropia, of which 9 cases were more hyperopic in the ptosis eye than in the fellow eye. And the anisometropia incidence was 0 in the patients with mild ptosis, 26.1% in those with moderate ptosis, and 36.4% in those who had severe ptosis, suggesting a significantly increased anisometropia incidence as the severity of ptosis aggravates (χ^2=7.886, P=0.019; Table 1, Figure 1B).

There were no significant differences in SER (Z=-1.161, P=0.246), spherical power (SPH; Z=1.893, P=0.058), AL (t=0.460, P=0.647), CR (t=-1.879, P=0.064), AL/CR ratio (t=-1.849, P=0.068) and frequency of myopia (χ^2=0.091, P=0.762) and hyperopia (χ^2=0.785, P=0.376) between the fellow and ptotic eyes (Table 2). The frequency of astigmatism (χ^2=9.848, P=0.002) and cylindrical power (CYL; Z=-2.50, P=0.003) were significantly higher in the ptotic eyes than in the fellow eyes (Table 2). The SER (H=12.506, P=0.006; Figure 2A), SPH (H=11.279, P=0.010; Figure 2B), CYL (H=11.144, P=0.011; Figure 2C), AL/CR ratio (F=4.104, P=0.009; Figure 4C) and frequency of hyperopia (χ^2=15.117, P=0.002; Figure 3B) and astigmatism (χ^2=13.183, P=0.004; Figure 3C) were significantly different among the ptotic eye subgroups and the fellow eye group (Table 2). Other parameters, such as AL (Figure 4A), CR (Figure 4B) and frequency of myopia (Figure 3A), did not exhibit significant differences among these groups (Table 2). The frequency of hyperopia

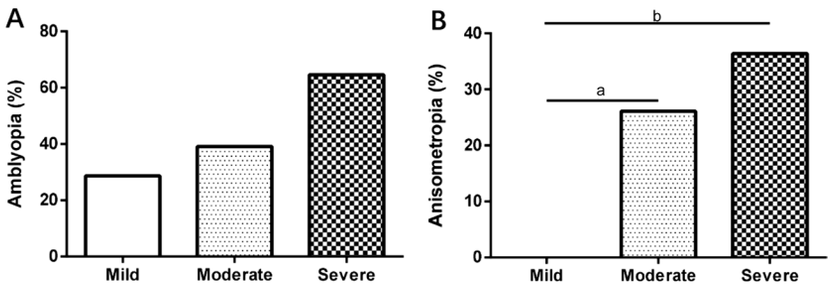

Figure 1 The ratio of amblyopia and anisometropia among the ptosis subgroups No significant difference in incidence of amblyopia (A) was found among the ptosis subgroups. A significantly increased anisometropia incidence (B) as the severity of ptosis aggravates. [a]$P<0.05$, [b]$P<0.01$.

Table 1 Demographics, amblyopia, and anisometropia in patients with congenital ptosis

Parameters	Total	Mild group	Moderate group	Severe group
Subject (*n*)	41	7	23	11
M:F ratio	28:13	5:2	16:7	7:4
Age (y)	7.78±3.28	8.57±2.76	7.91±3.29	7.00±3.69
Amblyopia	18 (43.9%)	2 (28.6%)	9 (39.1%)	7 (63.6%)
Anisometropia	10 (24.4%)	0	6 (26.1%)	4 (36.4%)

Table 2 Summary of patient data, measurement results in the normal and ptotic eyes

Parameters	Total	Fellow eye	Ptotic eye			
			Mild	Moderate	Severe	Total
Eye	82	41	7	23	11	41
Hyperopia	13 (15.9%)	20 (48.8%)	0	14 (60.9%)	10 (90.9%)	24 (58.5%)
Myopia	44 (53.7%)	7 (17.1%)	3 (42.9%)	3 (13%)	0	6 (14.6%)
Astigmatism	34 (41.5%)	10 (24.4%)	6 (85.7%)	11 (47.8%)	7 (63.6%)	24 (58.5%)
SER (D)	0.67±1.89	0.33±1.50	-0.91±2.29	1.13±1.98	1.96±1.89	1.00±2.17
SPH (D)	0.99±1.89	0.54±1.47	-0.21±2.18	1.47±2.00	2.41±2.05	1.43±2.17
CYL (D)	-0.64±0.74	-0.43±0.63	-1.39±1.14	-0.67±0.62	-0.91±0.75	-0.86±0.79
AL/CR ratio	2.91±0.15	2.94±0.13	3.00±0.19	2.88±0.16	2.80±0.12	2.88±0.16
AL (mm)	22.68±1.30	22.75±1.28	23.50±1.38	22.61±1.28	22.07±1.26	22.62±1.34
CR	43.26±1.61	43.59±1.49	43.06±0.80	42.94±1.68	42.84±2.15	42.93±1.68

SER: Spherical equivalent refraction; SPH: Spherical power; CYL: Cylindrical power; AL: Axial length; CR: Corneal curvature radius.

(Figure 3B) was significantly lower in mild group when compared with the normal eyes (χ^2=5.854, P=0.016), moderate ptotic eyes (χ^2=7.989, P=0.005) and severe ptotic eyes (χ^2=14.318, P=0.000). The group with severe ptosis showed higher frequency of hyperopia than the group with normal eye (χ^2=6.307, P=0.012). The frequency of astigmatism (Figure 3C) was significantly lower in normal group than those in the groups with mild ptosis (χ^2=10.118, P=0.001) and severe ptosis (χ^2=6.071, P=0.014). The SER (Figure 2A) was significantly lower in mild ptosis group than those in the groups with moderate ptosis (Z=-1.988, P=0.047) and severe ptosis (Z=-3.407, P=0.001). Moreover, the SER was significantly higher in the group with severe ptosis as compared with that in the normal eyes (Z=-2.753, P=0.006). The SPH (Figure 2B) was significantly higher in severe group when compared to the groups with mild ptosis (Z=-2.16, P=0.005) and normal eye (Z=-3.040, P=0.002). The CYL (Figure 2C) was significantly lower in normal group than those in the groups with mild ptosis (Z=-2.615, P=0.009) and severe ptosis (Z=-2.172, P=0.030). As for AL/CR ratio (Figure 4C), the value in the severe group was significantly lower, indicating a delayed eyeball development, when compared with those the normal eyes (t=2.716, P=0.007) and mild ptotic eyes (t=4.640, P=0.000). In patients with congenital ptosis, the ratio of AL/CR showed significantly positive correlations with the MRD-1 (r=0.464, P=0.002; Figure 5A), and negative correlations with the SER (r=-0.739, P=0.000; Figure 5B).

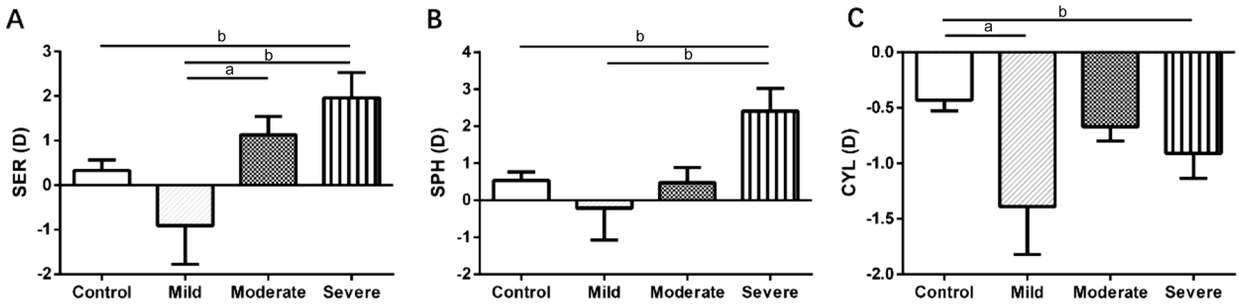

Figure 2 Comparisons of refractive parameters among the ptotic eye subgroups and the fellow eye group The SER (A), SPH (B) and CYL (C) were significantly different among the ptotic eye subgroups and the fellow eye group. [a]*P*<0.05, [b]*P*<0.01.

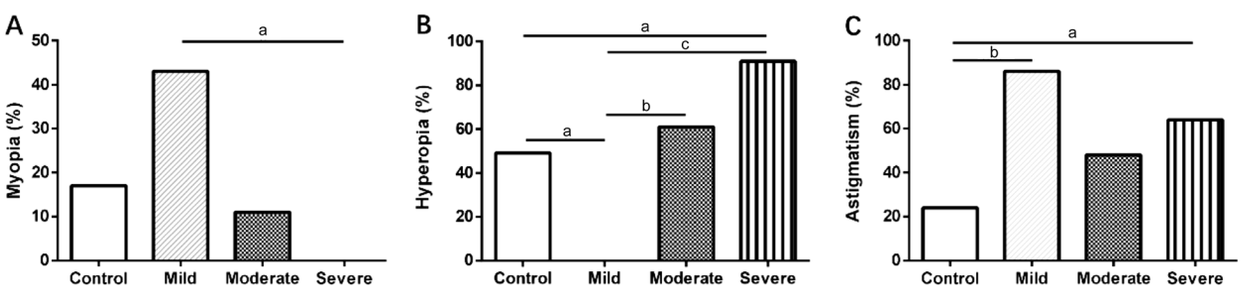

Figure 3 The ratio of myopia, hyperopia and astigmatism among the ptotic eye subgroups and the fellow eye group The differences in the frequency of myopia (A) did not reach statistical significance among the ptotic eye subgroups and the fellow eye group. The frequency of hyperopia (B) and astigmatism (C) were significantly different among the ptotic eye subgroups and the fellow eye group. [a]*P*<0.05, [b]*P*<0.01, [c]*P*≤0.001.

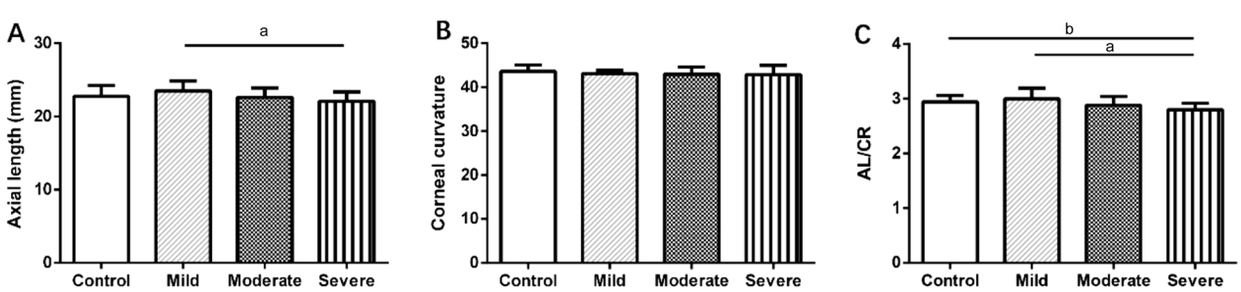

Figure 4 Comparison of parameters of AL/CR ratio among the ptotic eye subgroups and the fellow eye group There were no significant differences in AL (A) and CR (B) among the ptotic eye subgroups and the fellow eye group. The ratio of AL/CR (C) was significantly different among the ptotic eye subgroups and the fellow eye group. [a]*P*<0.05, [b]*P*<0.01.

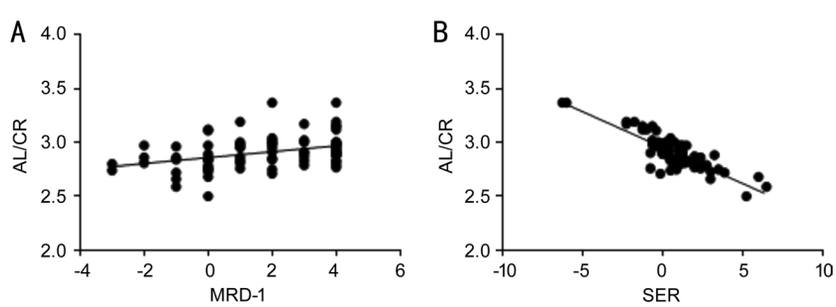

Figure 5 Correlations between MRD-1 and AL/CR ratio, SER and AL/CR ratio In the patients with congenital unilateral ptosis, the MRD-1 (A) was positively correlated with AL/CR ratio (r=0.464, P=0.002), and the SER (B) was negatively correlated with AL/CR ratio (r=-0.739 P=0.000).

DISCUSSION

In this study, we found that in eyes with unilateral congenital ptosis, the ratio of AL/CR is smaller and the refractive power is more hyperopic than in the fellow eyes. Especially, when the ptotic cases were further divided into mild, moderate, and severe, this phenomenon is more obvious, and has a

significant correlation with the severity of ptosis. In addition, the incidence of astigmatism, anisometropia, and amblyopia increased significantly. These results suggest that congenital ptosis may delay the development of eyeball, aggravate anisometropia, and increase the incidence of amblyopia in children with unilateral congenital ptosis.

It has been proposed that as the establishment of models of form-deprivation in animals[1-5], the risk of developing axial myopia increases dramatically, therefore, we would expect the parameters measured of eyeball in this study to become significantly axial myopic as congenital ptosis persist. However, this is not necessarily true based on our results, as no significantly difference in the AL between sides and among all subgroups was detected in children with congenital unilateral ptosis. This may due to a narrow palpebral fissure that allows light stimulation of the retina and the formation of clear retinal image is preserved, even in severe cases[6,9].

In the process of emmetropization in children, the changes in AL and CR are important biometric factors, and there is a compensating association between them[13]. The ratio of AL/CR has the strongest correlation with refractive error, and it is generally accepted that AL/CR ratios can be a helpful marker of the development of the eyeball[11-15]. Although, in our study, the AL/CR ratio and SER were not reaching a statistical significance between the ptosis and fellow eyes, we found AL/CR ratio is significantly lower and that SER is more hyperopic in the severe ptosis group than other groups when blepharoptosis was subgrouped according to the severity. Further, the AL/CR ratio exhibits a significant positive correlation with MRD-1 and a negative correlation with SER. These results suggest that ptosis may lead to a delay in the development of eyeball, particularly in children with severe unilateral congenital ptosis.

Amblyopia is the most common cause for losing monocular vision in children[19]. As revealed by our result and previous studies[20-22], the rate of amblyopia in children with congenital ptosis has been reported to be higher than that of the general population. Our data showed the incidence of amblyopia in children with congenital ptosis is 43.9%, significantly higher than general population (3.0% to 3.2%)[22]. According to previous studies[19-21], the causes of the increased prevalence of amblyopia in patients with congenital ptosis are probably due to a higher prevalence of refractive errors, anisometropia, strabismus and a form of occlusive stimulus deprivation. Indeed, we found, in the current study, that the incidence of anisometropia is 24.4% in children with congenital ptosis, and a significantly increased anisometropia incidence as the severity of ptosis aggravates. Furthermore, the frequency of astigmatism was significantly higher in the ptotic eyes than in the fellow eyes.

There are certain limitations in our study. First, this study included the preschool and school-aged children, and the difference of environmental and developmental factors may have affected parameters of eyeball such as AL, palpebral fissure height, and corneal shape[9,23-24]. In addition, myopia was relatively more prevalent in Asian children, while hyperopia in non-Hispanic white children[25]. Only Chinese subjects in the study was included is a limitation because the growth of eyeball differs according to ethnicity. Finally, we didn't investigate the ocular globe using other methods such as B-mode echography or optical coherence tomography that may provide more information. There are studies have demonstrated that morphological changes of the choroid were associated with the axial elongation in experimental animal models of form-deprivation[26-27], even in human eyes[28].

We conclude that congenital ptosis may lead to a delay in eyeball development in the aspect of AL/CR, further to aggravate anisometropia and increase the incidence of amblyopia in children, particularly in severe case. The findings of the present study suggest that children with unilateral congenital ptosis should be examined at regular intervals to detect refractive errors between eyes and suitable therapy, including spectacles, eye patches, and early surgical correction of ptosis to prevent the potential complications.

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