Comparison of ocular biometric parameters between concomitant exotropic and orthotropic eyes

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Research article

Abstract

Purpose

To compare the biometric characteristics between concomitant exotropia (XT) and orthotropia (OT) with OA2000.

Method

This cross-sectional study collected 4–18 years old children. All subjects underwent a comprehensive ophthalmic examination and prism alternate cover test for ocular alignment measurement. Included subjects had no any eye surgery, structural ocular anomalies, amblyopia of either eyes, ptosis, cataract and nystagmus. OA-2000 was used for the measurement of ocular biological parameters. Spherical equivalent (SE, spherical power + (cylindrical power)/2), keratometry, central corneal thickness (CCT), white to white distance (WTW), pupil diameter (PD), anterior chamber depth (ACD), lens thickness (LT), axial lengths (AL) and intereye differences in SE, keratometry, CCT, WTW, PD, ACD, LT and AL were analyzed by independent sample t-tests. Pearson correlation was used for correlations assessment. Partial correlation was used to control for intereye differences in SE.

Results

A total of 156 subjects (79 XT and 77 OT) were collected. Intereye differences in spherical equivalent (SE) (t 2.369, P 0.019), AL (t 3.423, P 0.001), ACD (t 3.782, P < 0.001), LT (t 3.136, P 0.002) and PD (t 3.229, P 0.002) were significantly larger in XT patients than OT patients. The correlation coefficient of XT with SE asymmetry was 0.187 (P 0.020), 0.265 with AL asymmetry (P 0.001), 0.289 with ACD asymmetry (P < 0.001), 0.251 with PD asymmetry (P 0.002) and 0.243 with LT asymmetry (P 0.002). Strong correlation (r 0.875) was found between anisometropia and AL asymmetry. After controlling the effect of anisometropia, the correlation coefficients slightly reduced between XT patients and intereye differences in AL (reduced to 0.213), ACD (reduced to 0.266), PD (reduced to 0.230) and LT (reduced to 0.230). Strong correlation (r 0.855) was found between intereye differences in ACD and LT.

Conclusion

Compared with OT subjects, intereye differences in SE, AL, ACD, LT and PD were significantly larger in XT patients and had positive correlation with XT and may be associated with the pathogenesis of XT.

Introduction

Concomitant exotropia (XT) is a manifest divergent strabismus and affects approximately 4% of adult population [1]which leads to the loss of binocularity and stereopsis. Besides functional effects, XT patients experience significant psychological stress, anxiety, and depression [2, 3]. XT often negatively impacts self-esteem, self-confidence and interpersonal relationships[4, 5]. Some patients assume adaptive techniques to hide extropia, such as placing their hair over the deviating eye[2]. Adults with

strabismus often have reduced quality of life[6], lower education levels, and lower chance on career choices[7].

The exact pathogenesis of XT has not been established although there are some reported risk factors such as maternal smoking during pregnancy[8], premature birth, perinatal morbidity, genetic anomalies[9], family history, anisometropia[10, 11] and myopia[12]. Among the reported risk factors, myopia and anisometropia have close correlation with ocular biometric parameters, especially in axial length [13–15]. To date, correlations between ocular bioparameters and XT remain unknown and no study has evaluated the biological parameters of XT. So we conducted the study hoping for finding some clue of the pathogenesis of XT using OA-2000.

OA-2000 (Tomey, Nagoya, Japan) is a novel non-contact and high-resolution optical biometric device. It incorporates swept-source optical coherence tomography and a Placido-disc topographer which can automatically find a measurable point and finish scans quickly and accurately. As a new biometer, OA2000 shows high repeatability and reproducibility, has excellent agreement with other optical biometric devices, such as IOL Master700 and Lenstar-LS900[16–20] and is widely used in accurate IOL power calculation[21]. The purpose of this study is to compare the biometric characteristics between XT and orthotropic (OT) patients using OA2000.

Methods

Ethical Approval

The study protocol adhered to the Declaration of Helsinki. Informed consents were obtained from the guardians of all subjects after the purpose of the study had been fully explained. The study was approved by the ethics committee of the Joint Shantou International Eye Center, Shantou University, Shantou, China.

Participants

Consecutive XT patients aged 4-18 years old were collected between July and August 2019 in Joint Shantou International Eye Center. All subjects underwent a comprehensive ophthalmic examination including visual acuity, intraocular pressure, cycloplegic refraction, anterior segment and fundus exam, corneal light reflex tests and prism alternate cover test (PACT) for ocular alignment measurement and OA-2000 for biometric parameters collection. Inclusion criteria included subjects with XT and OT. XT was defined as ≥15△ by PACT at distance or near fixation, while OT defined as ⬚15△ tested at distance or near fixation. Subjects with any eye surgery, structural ocular anomalies, amblyopia of either eyes, ptosis, cataract and nystagmus were excluded.

Visual acuity was measured using E International Visual Acuity Chart. Cycloplegia was obtained by using compound tropicamide eye drops in children more than 6 years old or atropine in 4-6-year-old subjects. Refractive status was recorded as spherical equivalent (SE, spherical power + (cylindrical power)/2).

Keratometry (K1, K2), central corneal thickness (CCT), white to white distance (WTW), pupil diameter (PD), anterior chamber depth (ACD), lens thickness (LT), and axial lengths (AL) were measured with OA-2000 before cycloplegia. Every subject had more than 8 results taken at one time with the single OA-2000 instrument and uniform ambient lighting conditions. Only measurements with high accuracy (SD less than 0.04 for keratometry, 0.02 for other parameters) and level A were acceptable otherwise retakens were needed. The intereye differences between these parameters were calculated as the absolute value of left minus right values.

Statistical Analysis

Data was analyzed using the software SPSS 21.0 (SPSS Inc., Chicago, IL, USA). Independent sample t-tests were used to compare age, refractive status, ocular biometric measurements and intereye differences. Nonparametric two Independent Samples test (Mann-Whitney U test) was used if equal variances were not assumed in Levene's Test. The associations were assessed using Pearson correlation and Partial correlation to control for anisometropia. The P level was set at 0.05.

Results

A total of 156 cases including 79 XT (mean age ± SD: 9.92± 3.32) and 77 OT (mean age ± SD: 8.97± 3.11) were collected. There were 32 females and 47 males in XT group and 36 females and 41 males in OT group. Intereye differences in SE (t 2.369, P 0.019) were significantly larger in XT patients (detailed in Table 1). No statistically significant differences were found in gender and age.

OA2000 Findings

No significance was found in Keratometry (K1, K2), CCT, WTW, PD, ACD, LT, and AL between XT and OT.

Intereye differences in AL, ACD, PD and LT were statistically significant in XT patients with equal variances not assumed. So, we reanalyzed these parameters with nonparametric independent samples tests founding that XT patients had larger intereye differences in AL, ACD, PD and LT (detailed in Table 1)

Table 1 Associations between XT and intereye differences in ocular parameters

	XT Mean (SD)	OT Mean (SD)	T value	P value	Mann-Whitney U test
SE asymmetry	0.878(0.931)	0.577(0.625)	2.369	0.019*	0.034
AL asymmetry	0.395(0.404)	0.208(0.265)	3.423	0.001*	0.000
ACD asymmetry	0.060(0.059)	0.032(0.030)	3.782	0.000*	0.001
PD asymmetry	0.557(0.476)	0.340(0.357)	3.229	0.002*	0.001
LT asymmetry	0.060(0.073)	0.031(0.035)	3.136	0.002*	0.003

XT: concomitant exotropia,

OT orthotropia,

SE: spherical equivalent,

AL: axial length,

ACD: anterior chamber depth,

PD: pupil diameter,

LT: lens thickness

*: results with equal variances not assumed and reanalyzed with Mann-Whitney U test

Correlation Analysis

Bivariate correlations revealed that XT patients had positive correlation with intereye differences in SE, AL, ACD, PD and LT. Intereye differences in SE namely anisometropia had positive correlation with XT, intereye differences in AL and ACD. Strong correlation (0.875) was found between anisometropia and intereye differences in AL. Intereye differences in PD namely anisocoria had positive correlation with XT, intereye differences in AL and LT. Strong correlation (0.855) was found between intereye differences in ACD and LT. (detailed in Table 2).

Table 2. Pearson Correlation and (P value) between XT and involved factors.

	XT	SE asymmetry	AL asymmetry	ACD asymmetry	PD asymmetry	LT asymmetry
XT	1	0.187 (0.020)	0.265 (0.001)	0.289 (0.000)	0.251 (0.002)	0.243 (0.002)
SE asymmetry	0.187 (0.020)	1	0.875 (0.000)	0.171 (0.033)	/	/
AL asymmetry	0.265 (0.001)	0.875 (0.000)	1	0.226 (0.005)	0.176 (0.028)	/
ACD asymmetry	0.289 (0.000)	0.171 (0.033)	0.226 (0.005)	1	/	0.855 (0.000)
PD asymmetry	0.251 (0.002)	/	0.176 (0.028)	/	1	0.198 (0.013)
LT asymmetry	0.243 (0.002)	/	/	0.855 (0.000)	0.198 (0.013)	1

XT: concomitant exotropia,

OT orthotropia,

SE: spherical equivalent,

AL: axial length,

ACD: anterior chamber depth,

PD: pupil diameter,

LT: lens thickness,

/: no correlation with P > 0.05

Partial Correlation Analysis to control for anisometropia

Strong correlation (r 0.735) [13]between anisometropia and AL asymmetry had been reported in non-XT subjects. So, we modified the statistical analysis using Partial correlation analysis to control for

anisometropia. The correlations slightly reduced but positive correlation was still evident between XT patients and intereye differences in AL (r 0.265 reduced to 0.213), ACD (r 0.289 reduced to 0.266), PD (r 0.251 reduced to 0.230) and LT (r 0.243 reduced to 0.230). Anisocoria had positive correlation with XT and LT asymmetry. Anisometropia had no influence on the strong correlation (0.855) between ACD and LT asymmetry (detailed in Table 3).

Table 3. Partial Correlation and (P value) between XT and involved factors when SE asymmetry controlled.

	XT	AL asymmetry	ACD asymmetry	PD asymmetry	LT asymmetry
XT	1	0.213 (0.008)	0.266 (0.001)	0.230 (0.004)	0.230 (0.004)
AL asymmetry	0.213 (0.008)	1	0.161 (0.046)	/	/
ACD asymmetry	0.266 (0.001)	0.161 (0.046)	1	/	0.855 (0.000)
PD asymmetry	0.230 (0.004)	/	/	1	0.187 (0.020)
LT asymmetry	0.230 (0.004)	/	0.855 (0.000)	0.187 (0.020)	1

XT: concomitant exotropia,

OT orthotropia,

SE: spherical equivalent,

AL: axial length,

ACD: anterior chamber depth,

PD: pupil diameter,

LT: lens thickness,

/: no correlation with P > 0.05

Discussion

In the present study, intereye differences in SE, AL, ACD, PD and LT were all significantly larger in XT patients than OT patients. XT patients had positive correlation with intereye differences in SE, AL, ACD, PD and LT.

Anisometropia defined as intereye asymmetry in refractive status had been reported to be associated with XT[15, 22-24]. On the other hand, early onset XT could lead to anisometropia due to the disruption of emmetropization process [25]. In our study, intereye differences in SE was significantly larger (0.878 vs 0.577) in XT patients. XT patients had larger intereye differences in AL, ACD, PD and LT. Correlations analysis revealed the positive correlation between XT and intereye differences in SE, AL, ACD, PD and LT. Anisometropia itself had been reported to be associated with lager intereye difference in AL and ACD[15]. To eliminate the influence of anisometropia, we modified the statistical analysis using Partial correlation and found that correlations between XT patients and intereye differences in AL, ACD, PD and LT were still statistically significant although the correlation coefficients were slightly reduced. Our study found that anisometropia had positive correlation with XT, intereye asymmetry of ACD and AL. Strong correlation (r 0.875) was found between SE asymmetry and AL asymmetry which was larger than 0.735[13] or 0.15[26] reported in non-XT subjects. Besides exotropic factors, reason for the differences between our findings and other reports may be the age range of the participants. Participants in other papers were adults while we studied 4-18 years old school-age children whose AL is gradually increasing and contributes to refractive errors.

Anisocoria is defined as intereye asymmetry in PD. 20% of normal people has physiologic anisocoria with no ocular and neurologic pathology [27, 28]. Larger contraction anisocoria appeared when stimulating the right eye and found in males [29, 30] which may be caused by brain asymmetry in visual cortices in male and lateralization toward the right hemisphere [31]. The relationship between anisocoria and XT or ocular biometric parameters is less frequently investigated in studies. In our study, all subjects had no history of ophthalmologic or neurological disease and physiologic anisocoria was found to be associated with XT. XT patients had larger PD asymmetry (0.557 vs 0.340) and positive correlation with anisocoria. We found no association between anisocoria and sex but positive correlation between anisocoria and AL asymmetry and LT asymmetry in XT patients. When controlling the effect of anisometropia, the correlation slightly reduced between anisocoria and XT (r 0.251 reduced to 0.230) and LT asymmetry (r 0.198 reduced to 0.187). No correlation was found between anisocoria and AL asymmetry.

LT as an important factor in anisometropia can contribute to refractive error and increases during accommodation [32]. Intereye asymmetry in LT reveals the accommodative difference between two eyes. Exotropia has been reported to be associated with decreased accommodation [33, 34]. In our study, intereye differences in LT was significantly larger (0.060 vs 0.031) in XT patients, indicating more intereye differences in accommodation. During accommodation, ACD decreased and LT increased [32] . Strong correlation (r 0.855) was found between intereye differences in LT and ACD in XT patients. The

correlation was not influenced by anisometropia. While weak or no correlation [15, 26]was found between LT and ACD asymmetry in non-XT patients.

Unlike other technologies such as diffusion-weighted imaging(DWI) which measures the motion of water diffusion across tissue and is particularly useful in tumor characterization [35, 36]and cerebral ischemia, optical biometry such as OA 2000 has been proven to be more accurate and safer [37, 38] for ocular biometric measurements. It incorporates SS-optical coherence tomography and a Placido-disc topographer which can automatically find a measurable point and finish scans quickly and accurately. As a new biometer, OA2000 has high repeatability and reproducibility. So only one measurement was taken for each subject which was timesaving. By OA 2000 measurements, we revealed that XT patients had larger intereye differences in SE, AL, ACD, LT and PD. On the other hand, subjects with larger intereye differences in SE, AL, ACD, LT and PD were prone to develop XT. Suggestions should be given to avoid or delay the development of XT.

Limitations to our study included its cross-sectional nature and subjects were not randomly selected. Among all parameters measured by OA 2000, measurements of PD should be adjusted manually by two technicians. Every subject in our study had only one measurement although more than 8 results were recorded. It was difficult to avoid all measurement biases even though OA2000 has high repeatability and reproducibility.

In summary, the current study firstly presented the biometric information in XT patients and found that XT may be correlated with anisometropia, anisocoria and intereye asymmetry in AL, ACD and LT. The data may aid in the etiology and management of XT.

Declarations

Authors' contributions: Weifen Gong: study designed, data collection and analysis, manuscript preparation; Fan Yang and Shibin Li: data collection, Geng Wang: study designed and manuscript preparation.

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