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Biometric investigation of ocular components in various types of anisometropia in school-age children

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学龄期儿童不同类型屈光参差眼球生物学参数的研究

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摘要

目的:比较学龄期儿童,不同类型屈光参差,双眼间视力及生物学参数的差异及其相关性。

方法:回顾性研究。纳入轻中度屈光参差的学龄期儿童(6-12 岁)128 例。根据屈光参差的类型分为 5 组。所有患儿均行睫状肌麻痹验光、眼部 A 超、角膜地形图检查。记录以下数据:屈光状态、最佳矫正视力(BCVA)、前房深度(ACD)、晶体厚度(LT)、玻璃体腔深度(VCD)、眼轴长度(AL)、角膜曲率半径(CR)、轴率比(AL/CR)。统计学分析采用 Kruskal-Wallis 检验和 Spearman 秩和检验。

结果:远视性屈光参差双眼间视力差异最大(0.14±0.20),近视性屈光参差双眼间眼球生物学参数 AL 和 VCD 差异最大(0.56±0.41,0.56±0.39 mm)。双眼间屈光参差和 BCVA、VCD、AL、AL/CR 呈正相关($P<0.05$),相关系数 r 分别为 0.266、0.379、0.350、0.263 与 LT、CR 无显著相关($r=-0.019$,-0.069,$P>0.05$)。然而在每个类型的组别中,屈光参差与双眼间的眼球生物学参数并无显著相关性。

结论:学龄期儿童远视性屈光参差在四种屈光参差类型中双眼视力差异最大。单纯远视或近视型屈光参差两眼间生物学参数的差异主要是由于 VCD 和 AL 的不对称,而散光型屈光参差双眼间的眼球生物学参数无显著差异。

关键词:屈光参差;远视;近视;散光;学龄期儿童

Abstract

• AIM: To compare the differences and correlations between different types of anisometropia, binocular visual acuity and biological parameters in school-age children.

• METHODS: A total of 128 school-age children (6-12 years) with mild-to-moderate anisometropia were retrospectively analyzed. Subjects were divided into five groups according to anisometropia type. All participants underwent cycloplegic refraction, A-scan ultrasound biometry, and corneal topography. Refractive status, best-corrected visual acuity (BCVA), anterior chamber depth (ACD), lens thickness (LT), vitreous chamber depth (VCD), axial length (AL), corneal radius (CR), and ratio of AL and CR (AL/CR) were recorded. Kruskal-Wallis and Spearman rank correlation tests were then used for statistical analysis.

• RESULTS: Hyperopic anisometropia had the greatest binocular vision difference (0.14 ± 0.20). Myopic anisometropia had the greatest asymmetry in AL and VCD (0.56 ± 0.41 and 0.56 ± 0.39 mm, respectively). Anisometropia was positively correlated with BCVA, VCD, AL, and AL/CR (r = 0.266, 0.379, 0.350, 0.263, respectively; $P < 0.05$), and it was not significantly correlated with LT and CR ($r=-0.019$, -0.069, respectively; $P > 0.05$), while no parameters had a statistically significant correlation with anisometropia in each group.

• CONCLUSION: School-age children with hyperopic anisometropia showed the greatest difference of binocular acuity in the four types of anisometropia. The inter-ocular differences of biometric parameters in simple hyperopic or myopic anisometropia were mainly attributed to the asymmetry of VCD and AL, while the differences in ocular parameters were not statistically significant in school-age children with astigmatic anisometropia.

• KEYWORDS: anisometropia; hyperopia; myopia; astigmatism; school-age children

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INTRODUCTION

Anisometropia occurs when there is a difference in refraction of one diopter (1.0D) or more, measured as a sphere or cylinder[1-4]. Many studies have asserted that anisometropia is associated with significant visual problems, including aniseikonia, strabismus, amblyopia, and stereopsis[5-7]. It is also challenging to diagnose as it is not readily apparent to primary care physicians or parents. Hence, treatment is often delayed. Studies have shown that the prevalence of anisometropia varies globally: in America, it varies from 5.8% to 15.0%; in Asia, it varies from 3.7% to 11.2%; and, in Europe, it varies from 4.6% to 6.9%[8].

Although the incidence of anisometropia and its relationship to amblyopia and ocular parameters have been well-studied[9-11], most researchers used spherical equivalent (SE) to calculate the degree of anisometropia[12-13], which ignores astigmatic error. Many others calculated anisometropia using the largest difference at any one meridian, which ignores spherical equivalent[14]. Other studies focused on the relationship between the degree of anisometropia and the depth of amblyopia[15-16]. Nevertheless, little is known about which type of anisometropia has the greatest impact on amblyopia. Furthermore, most previous studies did not measure or correlate corneal curvature and ocular biometrics in anisometropia patients. To the best of my knowledge, no study has delineated the relationship between the interocular differences of ocular biometric parameters in cases of anisometropia.

Therefore, the aim of this study was to investigate the differences of ocular biometric parameters between both eyes and explore the correlation of anisometropia based on those differences and visual acuity in school-age children. Doing so is very important for screening, diagnosis, prevention, and treatment of anisometropic amblyopia in children.

METHODS

Study Participants　This retrospective control study included 128 (256 eyes) school-age children who visited our hospital between January 1, 2019 and December 31, 2021, based on the following criteria: aged 6 - 12 years, anisometropia, no other eye diseases or abnormalities, no strabismus, no eccentric fixation, no microtropia, and no treatment of amblyopia. The subjects were divided into five groups according to anisometropia type: group 1 (spherical hyperopic), group 2 (spherical myopic), group 3 (cylindrical hyperopic), group 4 (cylindrical myopic), and group 5 (no anisometropia). Ethics Committee approval was granted by the Medical Science Department of Xi'an Jiaotong University, and the study conformed to the Declaration of Helsinki. All parents provided written consent.

Anisometropia Criteria　Significant anisometropia is defined as an SE interocular difference of more than 1.0D[1]. In our study, patients with anisometropia were divided into four types. Spherical hyperopic or myopic anisometropia is defined as a difference in hyperopia or myopic spherical refractive error of 1.0D or more between two eyes, and the inter-ocular differences of cylindrical is less than 1.0D. Cylindrical hyperopic or myopic anisometropia is defined as a difference in hyperopia or myopic cylindrical refractive error of 1.0D or more between two eyes, and the difference of spherical refractive error in binocular is less than 1.0D[17-19]. Non-anisometropic is defined as the spherical equivalent ≤0.5D[20]. The patients of this study were classified as either hyperopic or myopic based on the more ametropic eye. All patients with significant astigmatic error had cylindrical axes transformed to 180°. Therefore, the axis of astigmatism was not considered.

Procedures　Ocular examination: All patients underwent slit-lamp and fundus examinations *via* indirect ophthalmoscopy with pupil dilatation to exclude other ocular pathologies, such as ocular surface and fundus diseases. A cover-uncover test and synoptophore examination were then used to exclude strabismus. A careful review of the patents' medical histories was performed to ensure no previous ocular treatments or surgeries.

Visual acuity: Best corrected visual acuity (BCVA) was measured with a Snellen chart at a 5-m distance using the cover/uncover test by the same refractionist after cycloplegic refraction. For children who could not read the Snellen chart, the data were omitted. Note that there was no case in which a child could read only few letters without finishing the line. All data were recorded and transformed to LogMAR for statistical analysis.

Cycloplegic refraction: Subjects younger than 10 years old received 10 drops (within 3-7d) of 1.0% Atropine sulfate ophthalmic gel. Those 10 years of age or older received tropicamide phenylephrine drops five times every 10min and waited for 20min prior to assessment. Cycloplegic refraction was then performed by a senior refractionist in a dark room, the refraction states were recorded.

Biometry: A-scan ultrasound biometry (Topcon, Tokyo, Japan) was used to measure ocular biometric parameters [*i.e.*, anterior chamber depth (ACD), lens thickness (LT), vitreous chamber depth (VCD), and axial length (AL)]. One drop of proparacaine hydrochloride was added to each eye 1-2min prior to ultrasonography. The probe was placed lightly on the center of the cornea perpendicular to its axis with the patient in the supine position. The average value of at least 10 measurements (mm) for AL, ACD, LT, and VCD were recorded for each eye. All examinations were performed by the same experienced clinician.

Using corneal topography (TMS-4N, TOMEY, Japan), the mean of three keratometric readings were taken as K1 and K2, and the mean K value were calculated for both eyes. The corneal radius (CR) was calculated as CR = 337.5/[average keratometry (D)].The ratio of AL and CR(AL/CR) was also calculated.

Data Analysis　Nonparametric data analysis was performed using SPSS 23.0, the data were not normally distributed (sample Kolmogorov-Smirnov testing; $P < 0.05$). The Kruskal-Wallis test was used to identify statistically significant differences about the mean age of subjects and ocular parameters, including BCVA. Kruskal-Wallis pairwise tests were also used to compare differences between each group. The relationships between the amount of anisometropia and the interocular differences of ocular parameters and visual acuity were analyzed using Spearman's rank correlation coefficients. Statistical significance was defined as $P<0.05$.

RESULTS

A total of 128 children (256 eyes) aged 6-12 years were included in the analysis. The mean age was 7.97±1.71 years; 48.4% ($n=62$) were male, and 51.6% ($n=66$) were female. The subjects were divided into five groups, and basic demographics are shown in Table 1.The mean value of inter-ocular differences in variables, including refraction and ocular parameters in each group were shown in Table 2.

The gender ratio in each group was consistent, and Kruskal-Wallis testing showed that there were no statistically significant differences in the mean age ($P=0.386$) of subjects between groups.

The ocular parameters(BCVA, VCD, AL, and AL/CR) were found to be statistically significantly different ($P<0.05$), whereas ACD, LT, and CR showed no significant differences in all groups ($P>0.05$).

The total mean of the amount of anisometropia was 1.43±1.07 (ranging from 1.0D to 3.0D), and the mean values of each group were shown in Table 2. There were significant differences of refraction in all groups (Kruskal-Wallis test; $P=0.000$), then pairwise testing was used to determine whether there were significant inter-ocular differences of refraction, showing that groups 1-4 presented significant differences from group 5 ($P<0.05$). However, groups 1-4 showed no significant differences ($P>0.05$).

Hyperopic anisometropia (group 1) had the greatest difference of binocular acuity (0.14±0.20), followed by cylindrical hyperopic anisometropia (group 3: 0.09±0.14). The differences in myopic(group 2) or cylindrical myopic(group 4) anisometropia of binocular vision were not significant (0.03±0.07 and 0.02±0.51, respectively), whereas control group (group 5) was 0.01±0.03. The inter-ocular differences of visual acuity in group 1 or group 3 were statistically significant in the group 2 or group 4 and control group ($P<0.05$), whereas groups 1 and 3 had no statistically significant differences ($P=1.000$). When comparing group 2 or group 4 with the control group, there were no statistically significant differences ($P>0.05$). Groups 1 and 2, compared with groups 3 and 4, presented statistically significance differences of $P=0.005$ and 0.034, respectively, as analyzed by Kruskal-Wallis pairwise testing (Table 3).

AL and VCD were found to be statistically significantly different in all groups ($P<0.05$). Myopic anisometropia had the greatest asymmetry in AL and VCD (0.56±0.41 and 0.56±0.39mm, respectively), followed by hyperopic anisometropia (0.52±0.42 and 0.46±0.36mm, respectively). These two groups were not statistically significantly different ($P=1.000$).The inter-ocular differences of AL and VCD in hyperopic or myopic cylindrical anisometropia were also not significant (AL: 0.20±0.24 and 0.15±0.17 mm; VCD: 0.16±0.16 and 0.15±0.17mm, respectively). These two groups were also not statistically significantly different ($P=$

Table 1 Demographic data of the study group

Group	n	Age ($\bar{x}\pm s$, years)	Males	Females
G1	23	8.00±1.60	15 (65.2%)	8 (34.8%)
G2	28	8.43±1.60	16 (57.1%)	12 (42.9%)
G3	26	7.77±1.68	10 (38.5%)	16 (61.5%)
G4	23	7.83±1.75	8 (34.8%)	15 (65.2%)
G5	28	7.77±1.93	13 (46.4%)	15 (53.6%)
Total	128	7.97±1.71	62 (48.4%)	66 (51.6%)

G: Group.

1.000), and the control group was found to be 0.14±0.14 and 0.10±0.09mm. Kruskal-Wallis pairwise testing showed that groups 3 and 4 had no statistically significant difference from group 5 ($P>0.05$); whereas groups 1 and 2 were statistically significantly different from the control group ($P<0.05$).

Inter-ocular CR differences were found to be not statistically significantly different between groups, but the ratio of inter-ocular AL and AL/CR differences were statistically significantly different ($P<0.05$). The differences of AL/CR between the eyes in myopic anisometropia was the greatest (0.08±0.05), followed by hyperopic anisometropia (0.07±0.05).

Inter-ocular differences in ACD and LT were not statistically significantly different ($P>0.05$) in all groups. The mean values were 0.16±0.17and 0.13±0.15mm, respectively, for all groups. These values are shown in Table 2.

The relationships between the level of anisometropia with inter-ocular differences (BCVA, ACD, LT, VCD, AL, and AL/CR) were analyzed using the Spearman's rank test. The level of anisometropia was positively correlated with BCVA, VCD, AL, and AL/CR ($r=0.266$, 0.379, 0.350, and 0.263, respectively; $P<0.05$) in all groups. However, in each group, there were no statistically significant differences between the levels of anisometropia and all ocular parameters and visual acuity ($P>0.05$).

DISCUSSION

Best Corrected Visual Acuity In the field, there are differences with regards to correlating the depth of anisometropic amblyopia to differences in refraction between eyes. Some authors have found no relationship between the degree of anisometropia amblyopia and its depth[21-22]. However, others have noted strong relationships[23]. Cobb *et al*[24], in a retrospective analysis of 112 children with anisometropic amblyopia, observed that the amount of refractive error and degree of anisometropia strongly correlated with final visual acuity. Hefni and Osman[25] noted amblyopia to be more likely in hypermetropic rather than myopic anisometropia. These findings were later confirmed by Jampolsky *et al*[26], which aligns with ours, as we found hyperopia or cylindrical hyperopic anisometropia having the greatest inter-ocular differences in binocular acuity. However, in the cited study, the degree of anisometropia and depth of amblyopia were strongly correlated ($r=0.607$, $P<0.05$). In ours, the correlation was weak ($r=0.122$ and 0.318), and there was no statistically significant difference ($P>0.05$).

Table 2 The mean value of inter-ocular differences in variables and Kruskal-Wallis test $\bar{x}\pm s$

Group	SE (D)	BCVA (LogMAR)	ACD (mm)	LT (mm)	VCD (mm)	AL (mm)	CR (mm)	AL/CR (mm)
G1	2.26±1.37	0.14±0.20	0.24±0.26	0.16±0.17	0.46±0.36	0.52±0.42	0.05±0.05	0.07±0.05
G2	1.78±0.68	0.03±0.07	0.15±0.11	0.15±0.18	0.56±0.39	0.56±0.41	0.04±0.03	0.08±0.05
G3	1.55±0.74	0.09±0.14	0.16±0.21	0.13±0.18	0.16±0.16	0.20±0.24	0.06±0.06	0.04±0.03
G4	1.57±0.77	0.02±0.51	0.13±0.12	0.14±0.03	0.15±0.17	0.15±0.17	0.03±0.04	0.02±0.03
G5	0.29±0.27	0.01±0.03	0.12±0.09	0.11±0.08	0.10±0.09	0.14±0.14	0.07±0.08	0.04±0.04
Total	1.43±1.07	0.05±0.12	0.16±0.17	0.13±0.15	0.23±0.32	0.31±0.35	0.53±0.54	0.05±0.45
P	0.000[a]	0.000[a]	0.706	0.872	0.000[a]	0.000[a]	0.465	0.000[a]

SE: Spherical equivalent; BCVA: Best corrected visual acuity; ACD: Anterior chamber depth; LT: Lens thickness; VCD: Vitreous chamber depth; AL: Axial length; CR: Corneal radius; G: Group; D: Diopter; mm: Millimeter; [a]$P<0.05$ was considered to be statistically significant.

Table 3 The *P* value of ocular parameters for Kruskal-Wallis compare pairwise

Parameters	G1-2	G1-3	G1-4	G1-5	G2-3	G2-4	G2-5	G3-4	G3-5	G4-5
BCVA	0.005[a]	1.000	0.005[a]	0.001[a]	0.034[a]	1.000	1.000	0.034[a]	0.007[a]	1.000
VCD	1.000	0.018[a]	0.010[a]	0.000[a]	0.000[a]	0.000[a]	0.000[a]	1.000	1.000	1.000
AL	1.000	0.008[a]	0.002[a]	0.001[a]	0.000[a]	0.000[a]	0.000[a]	1.000	1.000	1.000
AL/CR	1.000	0.305	0.003[a]	0.058	0.006[a]	0.000[a]	0.000[a]	1.000	1.000	1.000

BCVA: Best corrected visual acuity; VCD: Vitreous chamber depth; AL: Axial length; CR: corneal radius; G: Group; [a]$P<0.05$ was considered to be statistically significant.

Table 4 Spearman's rank correlation coefficient for the amount of anisometropia and interocular differences variables

Group	BVCA	ACD	LT	VCD	AL	CR	AL/CR
G1	0.063	0.083	-0.001	0.225	0.215	0.061	0.150
G2	0.252	-0.194	-0.102	0.298	0.282	-0.209	0.259
G3	0.107	0.130	-0.220	0.135	-0.084	0.056	0.027
G4	0.313	0.164	0.122	0.194	0.207	-0.059	0.145
G5	0.046	-0.158	-0.204	0.122	0.225	-0.197	-0.112
Total	0.266	0.110	-0.019	0.379	0.350	-0.069	0.263
P	0.002[a]	0.217	0.832	0.000[a]	0.000[a]	0.439	0.003[a]

BCVA: Best corrected visual acuity; ACD: Anterior chamber depth; LT: Lens thickness; VCD: Vitreous chamber depth; AL: Axial length; CR: Corneal radius; [a]$P<0.05$.

This discrepancy may have been caused by the different criteria used to select subjects. In the cited study, all subjects had anisometropia amblyopia; whereas, in ours, the subjects only had anisometropia, including amblyopia and unamblyopia.

In the paper of Townshend *et al*[16], which investigated 303 subjects, aged 7-70 years, the differences in manifest refraction and amblyopia depth were found to be greater for myopic than hyperopic individuals. This result contradicts ours. According to Townshend, the retina of the more ametropic hypermetropic eye never receives a clear image; whereas, for myopic anisometropic patients, one eye can sometimes be used for near close-up work, and the less myopic eye can be used for distance observations. Therefore, with myopic anisometropia, either eye can produce a clear retinal image.

Therefore, we confirm that hyperopia or cylindrical hyperopic anisometropia is more strongly correlated with an inter-ocular difference of visual acuity than myopia, despite there being no statistically significant difference in our study ($P>0.05$). On the other hand, Malik *et al*[22] and Hedgpeth and Sullivan[27] both found no relationship between the degree of anisometropia and its depth in myopic, hypermetropic or astigmatic groups[22].

Axial Length and Vitreous Chamber Depth Differences between the AL of the two eyes contributed to anisometropia: more so in myopic cases[15]. The cited study included 85 cases of untreated anisometropic in subjects aged 7-50 years (mean = 24.95), divided into hypermetropic and myopic groups. The researchers found a strong positive relationship between the level of anisomyopia and the inter-ocular differences of AL (Pearson rank coefficient) for both hyperopic and myopic anisometropia ($r=0.609$ and 0.674; $P<0.001$). The correlation coefficients were found to be greater for myopic than hypermetropic anisomyopia individuals. These results are consistent with ours ($r=0.282$ and 0.215, respectively). We found no statistical significance in correlations ($P>0.05$). Ueki *et al*[28] used Pearson's correlation to show a negative correlation between the difference in SE and AL (-0.90; $P=0.00$). In our study, apart from group 3, we found negative correlations with inter-ocular differences and refraction; other groups presented positive correlations.

Inter-ocular differences in VCD showed high correlations with AL ($r=0.762$, $P=0.000$) with all groups in our study. The interocular differences in VCD between two eyes were found to have similar results as AL in each group. Presently, there are few reports about the VCD of anisometropia. Cass and Tromans[29] investigated 27 pre-school children with hyperopic anisometropic amblyopes, finding statistically and clinically significant differences in VCD when comparing eyes. The interocular difference in VCD was 0.77±0.92mm. In our study, the mean value was 0.46 ± 0.36mm for hyperopic anisometropia.

The varying results may have been caused by differences in statistical methods. Most previous used Pearson's rank correlation coefficient. However, for our data, it does not conform to a normal distribution. Hence, we used Spearman's rank correlation coefficient. Additional confusion has resulted from differences in anisometropia criteria. Most investigators defined anisometropia as ≥1.0D differences in SE, which fails to account for anisometropia types[30]. In our study, we separated types, considering the effect of astigmatic error. Additionally, the great age differences of the subjects examined in past papers should be considered.

Corneal Radius and Ratio of Axial Length and Corneal Radius With myopia, corneal curvature was found to play a minor role in ocular refraction, especially in mild-to-moderate cases[31]. Achieving emmetropia requires the regulation of AL growth to match the optics of the eye. An abnormal growth pattern results in a poor correlation between refraction and CR[32]. Zaka-ur-Rab[15] studied 85 cases of untreated anisometropic amblyopia in subjects aged 7-50 years, finding a relationship between the interocular differences of refraction and keratometry using Pearson's rank correlation coefficient ($r=-0.147$ and -0.020, respectively; $P>0.05$). However, in our study, inter-ocular differences of corneal radii were positive with refraction for hypermetropic cases ($r=0.061$, $P>0.05$); for myopic cases, the result contradicted that of Zaka-ur-Rab ($r=-0.209$, $P>0.05$) with no statistical significance ($P>0.05$). Cass and Tromans[29] investigated 27 preschool children in a hyperopic anisometropic amblyopes group, finding that the relationship between refraction and corneal curvature was significant ($r=0.34$, $P=0.004$) *via* Spearman's rank correlation. These results are consistent with ours in the hyperopic anisotropic group.

The AL/CR value is associated with the development of myopia and may be a more useful marker of progress than AL alone[33]. However, there have been few reports about AL/CR in anisometropia. In our study, the inter-ocular difference of AL/CR was positive with refraction in all groups ($r=0.263$, $P=0.003$), showing statistical significance. However, per group, there was no statistical significance ($P>0.05$).

Anterior Chamber Depth and Lens Thickness Cass and Tromans[29] investigated 27 subjects with hypermetropic anisometropia aged 7-50 years, finding interocular differences in ACD and crystalline LT (0.11±0.60 and 0.08±0.68mm, respectively). In our study, the mean hypermetropic anisometropia value was 0.24 ± 0.26 and 0.16 ± 0.17mm respectively. The differences in age may have been a contributing factor.

The relationship between inter-ocular differences of refraction and ACD and LT was not statistically significant ($P=0.217$ and 0.832, respectively) in all groups, and there was no correlation ($P>0.05$).

CONCLUSIONS

The results of our study suggest that for various types of mild-to-moderate anisometropia, hyperopic anisometropia has the greatest effect on binocular acuity in school-age children. The inter-ocular differences of VCD and AL can be attributed to the major asymmetry of spherical anisometropia; whereas, for astigmatic anisometropia, the differences in ocular parameters were not significant. The amount of anisometropia was positive correlated with BCVA, VCD, AL, and AL/CR, and no correlations were found with ACD, LT, and CR.

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