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CLINICAL RESEARCH / KLİNİK ARAŞTIRMA

Long-term Evaluation of the Anisohypermetropic Children: What Happens to Visual Acuity, Binocular Vision and Refraction?

Anizohipermetropik Çocukların Uzun Dönem Değerlendirilmesi: Görme Keskinliği, Binoküler Görme ve Refraksiyona Ne Olur?

Nazife Sefi Yurdakul[1], Hasan Aytoğan[2]

[1]Başkent University Zübeyde Hanım Hospital, Clinic of Ophthalmology, İzmir, Turkey
[2]University of Health Sciences Turkey, İzmir Tepecik Education and Research Hospital, Clinic of Ophthalmology, İzmir, Turkey

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Abstract

Objective: Refractive errors and their inappropriate correction may not only lead to deterioration visual acuity (VA) but also deteriorate binocular functions and then lead to strabismus since the binocular single vision (BOV) and VA are important in ensuring the parallelism of the eyes. In this study, we evaluated the changes in best corrected visual acuity (BCVA), BOV and refraction in anisohypermetropic children.

Methods: The records of anisohypermetropic children who were followed up between January 1999 and June 2019 were retrospectively reviewed. Detailed ophthalmological examination findings of the initial and last control with at least one year follow-up were obtained. BCVA was determined by the Snellen-chart letters and transformed to the logarithm of the minimum angle of resolution (logMAR). Binocular vision functions were evaluated using the Titmus and Worth 4-dot tests. The changes in BCVA, BOV and refraction were evaluated.

Results: Seventy-one patients were included in the study. While 39 patients were male, 32 patients were female. The mean age of patients was 74.31±40.51 (24-180) months at the first admission, the mean follow-up time was 67.75±47.8 (12-204) months. Amblyopia was seen in 68 (95.77%) eyes with higher refractive error and 38 (53.52%) eyes with lower refractive error at the first examination. The median BCVA of the eye with higher refractive error was 0.52 logMAR at the first examination and 0.10 logMAR for the last control ($p<0.001$). The median BCVA of the eye with lower refractive error was 0.10 logMAR at the first examination and 0.00 logMAR at the last control ($p<0.001$). BOV was detected in 7 patients (9.9%) at the first examination, while BOV vision was detected in 22 (31%) patients at the last examination ($p<0.001$).

Conclusion: The results show the importance of close follow-up and early treatment in anisometropic cases because of the negative influence of anisometropia on visual functions.

Keywords: Amblyopia, anisometropia, binocular vision

Address for Correspondence/Yazışma Adresi: Hasan Aytoğan MD, University of Health Sciences Turkey, İzmir Tepecik Education and Research Hospital, Clinic of Ophthalmology İzmir, Turkey
Phone: +90 534 308 05 23 **E-mail:** hasan_aytogan@hotmail.com
ORCID ID: orcid.org/0000-0002-2653-6562

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Öz

Amaç: Refraksiyon kusurları ve uygunsuz düzeltmeler sadece görme keskinliğini bozmakla kalmaz, aynı zamanda binoküler fonksiyonları bozar ve binoküler tek görme ve görme keskinliği gözün paralelliğini sağlamakta önemli olduğu için şaşılığa yol açar. Bu çalışmada, anizohipermetropik çocuklarda en iyi görme keskinliği, binoküler tek görme ve refraksiyon değişimlerini değerlendiridik.

Yöntem: Ocak 1999 ile Haziran 2019 arasında takip edilen anizohipermetropik çocukların medikal kayıtları retrospektif olarak incelendi. En az bir yıllık takipleri olan hastaların başlangıçtan sona kadar detaylı göz muayeneleri kaydedildi. En iyi görme keskinlikleri Snellen eşeliyle değerlendirildi ve minimum çözünürlük açısına dönüştürüldü. Binoküler görme fonksiyonları Titmus ve Worth-4 nokta testi ile değerlendirildi. Düzeltilmiş en iyi görme keskinliği, binoküler görme, refraksiyon değişimleri değerlendirildi.

Bulgular: Çalışmaya 71 hasta dahil edildi. Otuz dokuzu erkek iken 32'si kadındı. Hastaların ortalama yaşı ilk başvuruda 74,31±40,51 (24-180) aydı, ortalama takip süresi 67,75±47,8 (12-204) aydı. İlk muayanede 68 (%95,77) gözde yüksek refraktif kusur ile ve 38 (%53,52) gözde düşük refraktif kusur ile ambliyopi izlendi. Yüksek refraksiyon kusurlu gözlerin ilk muayanede medyan en iyi düzeltilmiş görme keskinliği (EDGK) 0,52 minimum çözünürlük açısının logaritması (logMAR) ve son muayenede 0,10 logMAR'dı (p<0,001). Düşük refraksiyon kusurlu gözlerin ilk muayanede medyan EDGK 0,01 logMAR ve son muayenede 0,0 logMAR'dı (p<0,001). İlk muayenede 7 hastada (%9,9) tespit edildi, son kontrolde 22 (%31) hastada binokuler görme tespit edildi (p<0,001).

Sonuç: Anizometropinin görsel fonksiyonlar üzerine negatif etkilerinden dolayı anizometropik hastalarda erken tedavi ve yakın takibin önemini göstermiştir.

Anahtar Kelimeler: Ambliyop, anizometropi, binoküler görme

Introduction

Anisometropia is a difference in refractive error equal to or more than 1.00 diopter (D) spherical and/or cylindrical between the two eyes. Reported anisometropia rates range from 1% to 4.7% in different studies[1-3]. During visual development, uncorrected anisometropia causes blurred visual input and may result in amblyopia, which occurs up to 6.1% of the population[4]. In spherical myopic anisometropia, amblyopia is unlikely to develop with the less ametropic eye is used for distant vision, whereas the more ametropic eye is used for near vision unless the more ametropic eye has extremely high refractive error. In hypermetropic anisometropia, the less ametropic eye may be able to achieve a clear retinal image in distant vision, but the more ametropic eye receives relatively blurred input and may not have a sharp image focused on the retina and may lead to amblyopia[4,5].

Refractive errors and their inappropriate correction may not only lead to deterioration visual acuity (VA) but also binocular functions and then strabismus since the binocular single vision (BOV) and VA are important in ensuring the parallelism of the eyes[6]. In this study, we evaluated the changes in best corrected visual acuity (BCVA), BOV and refraction in anisohypermetropic children.

Materials and Methods

This study was conducted in accordance with the Helsinki Declaration principles. The Ethical Committee of University of Health Sciences Turkey, İzmir Tepecik Education and Research Hospital (decision no: 2022/05-17, date: 16.05.2022) approved this study. The records of anisohypermetropic children who were followed up between January 1999 and June 2019 were reviewed retrospectively. Detailed full ophthalmological were examined at the initial and last controls with at least one year follow-up. The patients who had not regular recorded findings of examinations and with ocular and neurological disorders, ocular motility disorders, vertical deviation of more than 10 prism Ds, failed to comply with the ocular assessment, high accommodative convergence/accommodation ratio was excluded in the study.

Anisohypermetropia was defined as a refractive error of equal or more than 1.00 D spherical and/or cylindrical between the two eyes. Refraction was evaluated by the autorefractometer (Topcon KR-8100) 45 min after the instillation of cyclopentolate hydrochloride (Sikloplejin 1%, Abdi İbrahim İlaç San. ve Tic. AŞ, Turkey). Refractive errors were also calculated as spherical equivalent (spherical error plus half the cylindrical component). Anterior segment was assessed with slit-lamp biomicroscopy, fundus was examined using +90 D indirect lens following cycloplegic effect continued.

BCVA was determined by the Snellen-chart letters and transformed to the logarithm of the minimum angle of resolution (logMAR). Amblyopia was defined as a BCVA less than 0.10 logMAR in one eye and a difference of two or more lines between the two eyes. If occlusion therapy was recommended for children with amblyopia depending on patient age and amblyopia depth after two months prescribed

glasses, if necessary. Eye movements were examined at nine cardinal gaze positions. The deviation was measured in the primary position with and without correction for near and distance with prism cover or Krimsky tests. The deviation angle near fixation was used in data analysis. Binocular vision functions were evaluated using the Titmus and Worth 4-dot tests. Stereopsis ≥100 sec/arc and the presence of fusion were accepted as indicating BOV. The initial follow-up was performed for two months, and then generally performed every 6 months.

Statistical Analysis

Statistical analysis of data was carried out with the Statistical Package for Scientific Studies (SPSS) version 26, (IBM Corporation, Armonk, New York, United States). Normal distribution was assessed with Kolmogorov-Smirnov and Shapiro-Wilk tests, variance homogeneity with the Levene test. The Mardia test was used for the compatibility of multivariate data to a normal distribution. Independent samples t-test, One-Way ANOVA, paired samples t-test, Wilcoxon-signed ranks and Mc-Nemar tests were used to compare the variables, Pearson's correlation and Kendall's tau-b tests were used to examine the correlations. Linear regression was used to investigate the causality. For the change in binocular vision, Neural Network (Multilayer Perceptron) was used. Quantitative variables are shown as mean ± standard deviation (SD) and median (minimum/maximum). Qualitative variables were expressed as frequency and percentage (n%). Variables were analyzed at the 95% confidence level and a p-value of less than 0.05 was considered significant.

Results

The mean age of 32 female (45.1%) and 39 male (54.9%) patients was 74.31±40.51 months (range, 24-180 months) at the first admission. The follow-up time was 67.75±47.82 months (12-204 months). Demographic characteristics and clinical findings of the patients are presented in Tables 1 and 2.

The median BCVA of the eye with higher refractive error was 0.52 logMAR at the first examination and 0.10 logMAR at the last control examination ($p<0.001$). The median BCVA of the eye with lower refractive error was 0.10 logMAR at the first examination and 0.00 logMAR at the last control examination ($p<0.001$). We observed that the VA of both eyes increased statistically at the last examination compared with the first examination ($p<0.001$). Amblyopia was seen in 68 (95.77%) eyes with higher refractive error and 38 (53.52%) eyes with lower refractive error at the first examination and improved to 40 (56.34%) and 9 (12.68%) eyes with higher and lower refractive error at the last examination, respectively. Baseline VA ($p<0.001$; $r=0.632$) and age at the first presentation ($p<0.001$; $r=0.402$) were found to be the leading significant factors affecting VA.

BOV (100 sec/arc stereopsis and fusion) was detected in only 7 patients (9.9%) at the first examination, while BOV vision was detected in 22 (31%) patients at the last examination ($p<0.001$). The presence of strabismus, the age of first presentation and the number of anisometropia were effective in the change of BOV (normalized importance: 100%, 98.1%, 89.6%, respectively). Strabismus (exotropia =4, esotropia =57) was observed in 61 cases (85.91%), orthotropia was observed in the remaining 10 cases (14.08%). During the follow-up, 17 patients (23%) of the cases in the study underwent strabismus surgery. The mean hypermetropic values of eyes with high refractive error at the first and last examinations were 4.89±2.01 and 4.60±1.93 D, respectively. A statistically significant decrease was observed in the hypermetropic values of eyes with high refractive error ($p=0.015$). The mean spherical equivalents of eyes with high refractive error were 5.43±1.91 D at the first examination and 5.27±1.88 D at the last examination (Graphics 1 and 2). Although there was a decrease in spherical equivalents, no statistically significant difference was observed ($p=0.171$). The median astigmatic values of eyes with high refractive error at the first and last examination were 0.75 and 1.00 D, respectively, and a statistically significant increase was observed in astigmatic values ($p=0.013$).

The mean hypermetropic values of eyes with lower refractive error at the first and last examinations were 3.25±2.14 and 3.22±2.05 D, respectively ($p=0.816$). The mean spherical equivalents of eyes with lower refractive error were 3.61±2.23 D at the first examination and 3.66±2.23 D at the final examination ($p=0.722$). The median astigmatic values of eyes with lower refractive error at the first and last examinations were 0.50 and 0.50 D, respectively ($p=0.124$). There was no significant difference between the hypermetropic, spherical equivalent, and astigmatic values at the first and the last examination ($p>0.05$) (Graphic 3). While a significant difference was observed between the hypermetropic and spherical equivalent anisometropia values at the first and the last examination ($p<0.05$), there was no difference between the astigmatic anisometropia values ($p=0.160$). When the age at presentation was divided into 24-60

months and 60-184 months; the mean spherical equivalent anisometropia values of the eyes with high refractive error at the time of presentation were 5.28±1.51 D for 24-60 months, 5.56±2.21 D for 60-184 months, and 3.4±1.88 and 3.76±2.49 D, respectively, for, for eyes with lower refractive error. There was no significance correlation between the age of presentation and the spherical equivalent difference, but, the higher the age of presentation, the larger the spherical equivalent difference.In regression analysis; high hypermetropic values were positively correlated with high spherical equivalent anisometropia (correlation coefficient r=0.784, p<0.001). It was also observed that initial low hypermetropic values were associated with low spherical equivalent anisometropia (correlation coefficient r=0.859, p<0.001, Table 3). When the correlation coefficients were compared, it was seen that the relationship between low hypermetropic values and low anisometropia was stronger (91.5%) than the relationship between high hypermetropia and high anisometropia (84.9%, Table 4).

Table 1. Demographic characteristics of anisohypermetropic children

	Mean ± SD (min/max)
Age at first admission (month)	74.31±40.51 (24/180)
Follow-up (month)	67.75±47.82 (12/204)
Gender	**n (%)**
Female	32 (45.1%)
Male	39 (54.9%)
Strabismus	
No	10 (14.1%)
Infantile esotropia	5 (7.1%)
Acquired esotropia	52 (73.2%)
Exotropia	4 (5.6%)
Strabismus surgery	17 (23.9%)
SD: Standard deviation, Min: Minimum, Max: Maximum	

Discussion

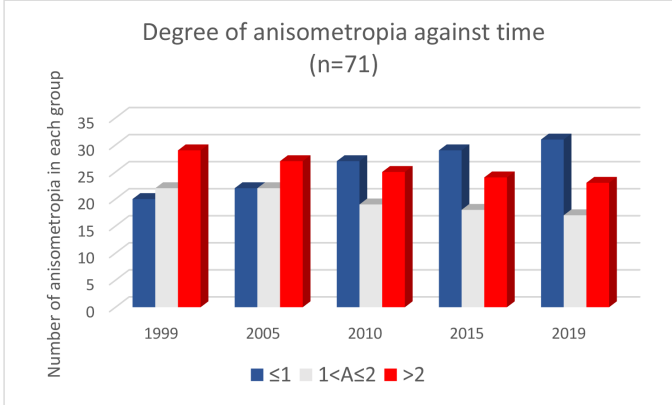
Anisometropia is an important risk factor for amblyopia, subnormal binocularity and strabismus. The rates of

Table 2. Clinical findings of anisohypermetropic children at the first and last examination

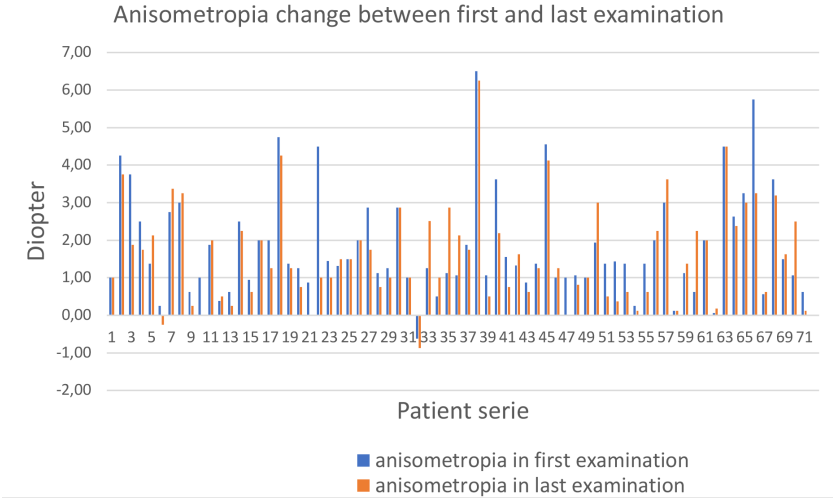
	First examination	**Last examination**	**p**
	Mean ± SD	**Mean ± SD**	
The eyes with high refractive error (D)			
Spherical equivalent	5.43±1.91	5.27±1.88	0.171[pt]
Hypermetropia	4.89±2.01	4.60±1.93	**0.015[pt]**
	Median (min/max)	**Median (min/max)**	
Astigmatism	0.75 (0.00/5.25)	1.00 (0.00/5.50)	**0.013[w]**
Visual acuity (logMAR)	0.52 (0.05/1.80)	0.10 (0.00/1.40)	**<0.001[w]**
	Mean ± SD	**Mean ± SD**	
The eyes with low refraction (D)			
Spherical equivalent	3.61 ± 2.23	3.66 ± 2.23	0.722[pt]
Hypermetropia	3.25 ± 2.14	3.22 ± 2.05	0.816[pt]
	Median (min/max)	**Median (min/max)**	
Astigmatism	0.50 (0.00/3.50)	0.50 (0.00/5.50)	0.124[w]
Visual acuity (logMAR)	0.10 (0.00/1.00)	0.00 (0.00/0.40)	**<0.001[w]**
Anisohypermetropia (D)			
Spherical equivalent	1.37 (-0.63/6.50)	1.38 (-0.88/6.25)	**0.011[w]**
Hypermetropia	1.37 (-2.25/6.50)	1.25 (-2.50/5.75)	**0.005[w]**
Astigmatism	0.13 (-2.00/4.75)	0.25 (-1.50/5.00)	0.160[w]
Deviation angle (PD)	14.00 (0.00/55.00)	0.00 (0.00/30.00)	**<0.001[w]**
	n (%)	**n (%)**	
Binocular single vision	7 (9.9)	22 (31.0)	**<0.001[m]**

[pt]Paired t test (Bootstrap), [w]Wilcoxon signed ranks test (Monte Carlo), [m] McNemar (Monte Carlo).
SD: Standard deviation, Min: Minimum, Max: Maximum, D: Diopter, PD: Prism diopter, logMAR: Logarithm of the minimum angle of resolution

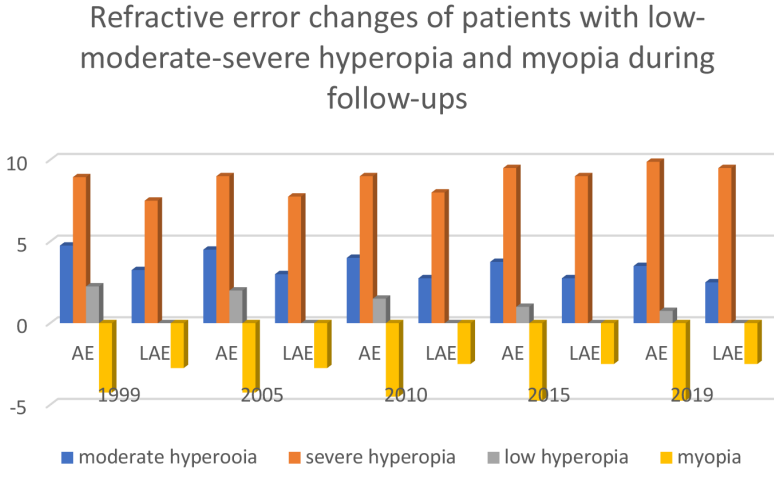
amblyopia in anisometropic patients have been reported to be up to 65.7%[3,6-10]. The differences in the results of the studies may be caused by the definition of anisometropia ranging from 1 D to 2 D and age at first admission. Kirandi et al.[8] observed that amblyopia was significantly associated with a higher amount of anisometropia. Rather than the amount of anisometropia, there are also studies showing the effectiveness of anisometropia type on amblyopia. Garcia et al.[3] noted that amblyopia is more common (55.6%) in patients with hypermetropic anisometropia. In this study, ≥1 D was taken as the anisometropia criteria and included only hypermetropic cases to ensure homogeneity. In the eyes of the higher and lower refractive error; amblyopia rates improved from 95.77% and 53.52% to 56.34% and 12.68%,



Graphic 1. Degree of anisometropia against time



Graphic 2. Absolute anisometropic changes against time



Graphic 3. Refractive error changes of four patients with low-moderate-severe hyperopia and myopia during follow-ups

respectively, following amblyopia treatment with both optical correction and occlusion according to the age of the cases. It was observed that BCVA of both eyes increased and amblyopia rates decreased statistically significant at the last examination compared with the first. Baseline VA and age at the first presentation were found to be the leading significant

Table 3. The changes of spherical equivalent difference in anisohypermetropic children

	High spherical equivalent difference	p	Low spherical equivalent difference	p
	r		r	
Age at first admission (month)	-0.062	0.466	-0.158	0.062
Follow-up (month)	0.030	0.724	-0.014	0.866
High anisohypermetropic difference	0.784	**<0.001**	0.421	**<0.001**
High anisoastigmatic difference	0.145	0.089	0.220	**0.010**
Low anisoastigmatic difference	0.277	**0.001**	0.337	**<0.001**
Low anisohypermetropic difference	0.492	**<0.001**	0.859	**<0.001**
Deviation angle difference	-0.072	0.402	-0.021	0.804
	Mean ± SD		**Mean ± SD**	
Gender				
Male	-0.03±0.87	0.227	0.05±1.00	0.970
Female	-0.32±1.08		0.04±0.99	
Strabismus surgery	-0.16±1.12	0.997	0.05±0.83	0.978
Increase in binocular vision	0.18±0.93	0.989	0.07±0.89	0.947

Kendall"s tau-_b test, iIndependent t- test (Bootstrap), One-Way ANOVA (Robuts statistic: Brown-Forsythe).
r: Correlation coefficient, SD: Standard deviation

Table 4. Regression analysis of the changes in anisometropic values

Independent variables	**B (SE)**	**p**	**Significance**
Difference			
High hypermetropia	1.002 (0.004)	**<0.001**	84.9%
High astigmatism	0.507 (0.005)	**<0.001**	11.6%
Low hypermetropia	-1.883 (0.059)	**<0.001**	1.2%
Low spherical equivalent	1.880 (0.059)	**<0.001**	1.2%
Low astigmatism	-0.933 (0.032)	**<0.001**	1.1%
Constant	0.002 (0.003)	**0.534**	
The dependent variable: High spherical equivalent difference		R^2=0.999	p model <0.001
Independent variables	**B (SE)**	**p**	**Significance**
Difference			
Low hypermetropia	1.001 (0.002)	**<0.001**	91.5%
Low astigmatism	0.498 (0.003)	**<0.001**	7.4%
High spherical equivalent	0.500 (0.016)	**<0.001**	0.4%
High hypermetropia	-0.501 (0.016)	**<0.001**	0.4%
High astigmatism	-0.252 (0.009)	**<0.001**	0.3%
Constant	-0.001 (0.002)	**0.559**	
The dependent variable: Low spherical equivalent difference		R^2=1	p model <0.001

R^2: Explanatory level of the model. Linear regression (Enter and Backward methods).
B: Rregression coefficient, SE: Standard error

factors affecting VA. Our results revealed that optimal success at desired levels may not be achieved in amblyopia treatment of those children with a delay in treatment and baseline low VA, as specified by Leon et al.[10] and Caputo et al.[9], respectively.

Besides to VA, BOV is also affected by anisometropia. The mechanism for subnormal binocularity can be the suppression of scotoma in the anisometropic eye[11]. Higher anisometropia was associated with poorer BOV. Weakley[6] reported that hypermetropic anisometropia more than 1 D and astigmatic anisometropia more than 1.5 D result in a significant increase in the incidence of amblyopia and a decrease in the stereoacuity. However, according to Kim and Kim[12] early refractive correction is more important than the amount of refraction. In this study, similar to the increase in BCVA; the BOV rates were significantly found to have increased at the last examination compared with the first, from 9.9% to 31%. The fact that most of our cases (73.2%) were refractive esotropia occurring in the non-critical period shows the importance of early correction that leads to the development of BOV[12,13]. We observed that the presence of strabismus, the age of first presentation and the number of anisometropia were effective in the change of BOV, respectively anisometropic cases may be with strabismus since the stereoacuity is one of the important factors that provide the parallelism in the eyes, as mentioned by Wilson et al.[14]. Phillips[15] emphasized that esotropia can occur in cases of hypermetropic anisometropia over 4 D. Duman et al.[16] observed that the risk of developing esotropia increased significantly in patients with high spherical anisometropia, between 1.5-4 D and over. Kim and Kim[12] reported that BOV obtained from early refractive correction, rather than the amount of refraction, is important in decreasing and controlling deviation. The development of esotropia in 80% of our anisohypermetropic cases supports the studies that suggest a relationship between the hypermetropia and esotropia. We also investigated the changes in refraction and anisometropia. In eyes with high refractive error; a significant decrease in hypermetropic and increase in astigmatic value changes is observed at the final examination compared to the first. When the astigmatic values were ranked increasingly, it was observed that the hyperopic value decreased as the astigmatic value increased. This inverse relationship may explain why high astigmatic values are not associated with higher spherical equivalents and therefore, the amount of spherical equivalent change is not significant. On the other hand, in eyes with lower refractive error; there was no significant difference between the hypermetropic, spherical equivalent, and astigmatic values at the first and the last examinations. A directly proportional relationship was also observed between astigmatic and hypermetropic values. The increase in hypermetropic and astigmatic value increases the spherical equivalent. We can say that the inverse relationship between astigmatism and hypermetropic values in eyes with high refractive error and the correct proportional relationship in eyes with lower refractive error balance the increase in the spherical equivalent differences between the two eyes, preventing the deepening of amblyopia. According to the study of Shih et al.[17], children with anisometropia had myopization and decreased in hypermetropia in both eyes of the hyperopic children. Yang et al.[18] pointed out that the full correction may increase the refractive error with a possible negative effect on emmetropization. Ingram et al.[19] who claimed that an inherent problem in these children could disturb the process of emmetropization. In terms of anisometropia, Yamashita et al.[2] revealed in their study that 84.3% of children had remained unchanged while 15.7% showed a significant increase or decrease in the amount of anisometropia with increasing age. Shih et al.[17] reported that myopic anisometropia decreases significantly over time, but hypermetropic anisometropia remains constant. In this study, while a significant difference was observed between the hypermetropic and spherical equivalent values at the first and the last examination, there was no difference between the astigmatic anisometropia values. When taking age into account; even though no significance correlation was observed between the age at presentation and the spherical equivalent difference, the higher the age presentation, the larger the spherical equivalent difference. Initial hypermetropic values were positively associated with spherical equivalent anisometropia. The relationship between low hypermetropia and low anisometropia was stronger than the relationship between high hypermetropia and high anisometropia. The absence of a significant difference in refractive changes of eyes with low refraction indicates that these eyes are more stable than the eyes with high refractive error. So, the eyes with high refractive error should be monitored closely.

Study Limitations

The major limitations of the study were the retrospective nature and the relatively small sample size. However, homogeneity provided by considering only hypermetropic anisometropia cases and long follow-up time composes the study strength.

Conclusion

In conclusion, the results show the importance of close follow-up and early amblyopia treatment in anisometropic cases because of the negative influence of anisometropia on visual functions.

Ethics

Ethics Committee Approval: The Ethical Committee of University of Health Sciences Turkey, İzmir Tepecik Education and Research Hospital (decision no: 2022/05-17, date: 16.05.2022) approved this study.

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: N.S.Y., H.A., Concept: N.S.Y., H.A., Design: N.S.Y., H.A., Data Collection or Processing: N.S.Y., H.A., Analysis or Interpretation: N.S.Y., H.A., Literature Search: N.S.Y., H.A., Writing: N.S.Y., H.A.

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