Anisometropia Magnitude and Amblyopia Depth in Previously Untreated Unilateral Amblyopia Patients

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Abstract

Objective: The study aimed to investigate the association among the depth of amblyopia, the magnitude of anisometropia, age, sex and laterality. **Methods:** A retrospective review of 13,146 patients was performed and 64 patients with unilateral anisometropic amblyopia were investigated between January 2013 and May 2015 in Hakkari Government Hospital Eye Clinic during my obligatory duty as an ophthalmologist. The depth of amblyopia, the magnitude of refractive error and anisometropia, age, laterality and gender of the patients were statistically analyzed. **Results:** Age was positively correlated with the cylindrical values of myopic amblyopic patients whereas such correlation was not observed in hyperopia (rho: 0.666; p < 0.01; Correlation is significant at the 0.01 level, 2-tailed). The amblyopia depth was significantly more common in the left eye compared to the right eye in severe and moderate amblyopia groups. In astigmatism, cylindrical powers of amblyopic eyes were statistically correlated with logMAR visual acuities of amblyopic eyes. The spherical powers of amblyopic eyes were statistically correlated with logMAR visual acuity of amblyopic eyes in myopia and in hyperopia. Also in hyperopia, cylindrical powers of healthy eyes were statistically correlated with cylindrical powers of amblyopic eyes (rho: 0.763; p < 0.01). This result may indicate the tendency of making amblyopia in both eyes of hyperopia patients. **Conclusion:** Refractive disorder difference of 0.75 diopter (D) astigmatism or 1.5 D of spherical refractive disorder difference was enough for amblyopia development. The same amount of anisohyperopia and anisoastigmatism leads to deeper amblyopia compared to the same amount of anisomyopia. The vision per D values of refractive disorders were approaching to each other above 4 D of spherical equivalents. The deeper amblyopia was significantly more common in the left eye compared to the right eye. The hyperopia seems to change slowly whereas the astigmatism and the myopia behave like a factor that varies as time goes by.

1. Introduction

The Greek words *amblyos* means dull, and *opia* means vision. Amblyopia refers to the decrease in best-corrected visual acuity in an eye having no organic pathology [1] and has to be treated within the sensitive period for visual development [2]. Amblyopia is associated with complete or partial lack of clear visual input to one eye (stimulus deprivation amblyopia or unilateral/anisometropic refractive amblyopia), or less often to both eyes (bilateral refractive amblyopia) or to conflicting visual inputs to the two eyes (strabismic amblyopia) [3]. Anisometropia is one of the main causes of amblyopia [4]. The difference in refractive error between two eyes produces abnormal binocular interaction and motivates inhibition of the eye with greater refractive error, resulting in a reduction in its visual acuity.

The cumulative incidence of amblyopia is estimated to be between 2% and 4% in children aged up to 15 years old [3]. Anisometropia, the asymmetry of refraction between fellow eyes, is an underdiagnosed cause of amblyopia because it is not readily apparent to parents or the child. As a result, it often goes undetected until the child is older [5]. If anisometropia is left untreated, it becomes a well-known amblyogenic factor [6].

Weakley found that the incidence and the depth of amblyopia were associated with the type and the magnitude of anisometropia. The risk of amblyopia is high in anisometropia if it is more than 2.00 D in myopia, more than 1.00 D in hyperopia and more than 1.50 D in astigmatism [7]. Younger children with anisometropia were found to have lower prevalence and depth of amblyopia in comparison to older children [8] whereas accompanying esotropia augmentates the depth of amblyopia [9].

In unilateral anisometropic amblyopia, the reduction of visual acuity in only one eye may not have a great impact on most of these children's daily life. This may result late presentation of patients to the hospital. Physicians may have trouble in evaluating possible least best corrected visual acuities and impairment scores of amblyopic patients. Clinicians can predict the patients' least possible best corrected visual acuity in unilateral refractive amblyopia. We investigated the best corrected visual acuities and depth of amblyopias, comparing it with such factors including age, sex, type, laterality and amount of refractive error in the previously untreated anisometropic amblyopia patients.

2. Methods

A retrospective review of 13,146 patients was performed which were between 2013 January and 2015 May in Hakkari Government Hospital Eye Clinic during my obligatory duty as an ophthalmologist. 134 patients had bilateral refractive amblyopia and 64 subjects were included into the study with the diagnosis of unilateral anisometropic refractive amblyopia without any treatment before. Unilateral refractive anisometropic amblyopia was secondary to refractive error differences between eyes. Anisometropic amblyopia develops when unequal refractive error in the two eyes causes the image on one retina to be chronically more defocused than the fellow eye. This form of amblyopia may occur in combination with strabismus but none of our patients had any deviation in their eyes.

All subjects had a comprehensive eye examination for visual acuity test for distance by Snellen chart, cycloplegic refraction and cover test for near and distance. Instillation of 1% cyclopentolate three times at a 10-minute intervals were performed, cycloplegia was considered completed as the neutralizing power of the retinoscopy was same at near and far. Cycloplegic refraction was performed by auto-kerato-refractometer (Topcon®, KR800) after 45 minutes time. Full refractive correction was prescribed and visual acuities were noted at the first visit and three weeks after the prescription. Patients were diagnosed with amblyopia whether if their inter-ocular visual acuity differences were 1 and more Snellen lines and amblyopia was classified mild, moderate and severe according to the both refraction values and visual acuities. All individuals were orthotropic and all of them had healthy ocular structures except two of them had bilateral tilted disk. None of the patients had any degenerative changes on fundus examination or any other ocular pathology such as cataract formation, glaucomatous cupping or peripapiller atrophy. Based on the amount of refractive error, we classified each refractive error as mild (myopia: −0.50 D to −3 D; hyperopia: +0.50 D to +3 D; astigmatism: 0.50 D to 1 D), moderate (myopia: −3 D to 6 D; hyperopia: +3 D to +6 D; astigmatism: 1 D to 2 D), or severe (myopia: −6 D and over; hyperopia: +6 D and over; astigmatism: 2 D and over) Depending upon the axis of cylindrical component, astigmatism was classified as with the rule (axis 61 - 119), against the rule (axis 0 - 29 and 151 - 180), or oblique (axis 30 - 60 and 120 - 150). Based on the best corrected visual acuity of the amblyopic eye, amblyopia was classified as mild amblyopia (8/10 to 9/10), moderate amblyopia (4/10 to 6/10) or severe amblyopia (worse than 4/10). Associations between the depth of amblyopia and the age and/or gender of the subjects, the laterality of the amblyopic eyes, the type and the magnitude of the refractive error of the amblyopic eyes and the magnitude of anisometropia were statistically analyzed. Astigmatisms of patients were transformed to minus cylinder to facilitate the statistical analysis. Data were analyzed using SPSS 20 software. Shapiro-Wilk test was applied to determine the normality of the variables. We used non-parametric tests because our values were non-normal in distribution. Chi-square test, two-sided Spearman's correlation and one-way

ANOVA tests were performed. A p-value of less than 0.05 was considered as statistically significant. Informed consent was obtained from all patients and ethics approval was granted by the local ethics committee. The research adhered to the tenets of the Declaration of Helsinki.

3. Results

The study included 64 patients with unilateral anisometropic amblyopia. The number of females (70.3%, n = 45) was bigger than the number of males (29.7%, n = 19). The mean age of patients was 21.33 ± 9.27 ranging from 5 to 46. The median age was 14 years old. Of all subjects, 31.2% were diagnosed with severe amblyopia, 59.4% with moderate amblyopia and 9.4% with mild amblyopia according to the visual acuities. For all three types of refractive error, mild refractive error was found in 34.4% of eyes, moderate error was found in 39% of eyes and high refractive error was found in 26.6% of eyes. The amblyopia frequency was 38 (59.4%) in the left eye and 26 (40.6%) in the right eye. The deeper amblyopia was significantly more common in the left eye compared to the right eye (Pearson Chi-Square, 2-sided p < 0.05) This statistically result was evident in moderate and severe amblyopia according to both the refractive state and visual acuity. But there was not any statistically correlation for the depth of amblyopia between gender or type of refractive error.

The astigmatism was found to be the most common type of refractive error, comprising 53.1% of the amblyopic eyes followed by hyperopia 25% and myopia 21.9%. Against the rule astigmatism was found in majority of the eyes with astigmatism (67.2%, n = 43 versus 17.2%, n = 11 with the rule and 15.6%, n = 10 oblique); however, severity of amblyopia was not statistically correlated with the type of refractive error or type of astigmatism.

In astigmatism, cylindrical powers of amblyopic eyes were statistically correlated with logMAR visual acuities of amblyopic eyes (rho: 0.652; p < 0.01). Spherical equivalents of amblyopic eyes were statistically correlated with logMAR visual acuities of amblyopic eyes in astigmatism (rho: 0.370; p < 0.05). The differences of spherical eqivalents between amblyopic eyes and healthy eyes were statistically correlated with the differece of logMAR visual acuities of amblyopic eyes and healthy eyes (rho: 0.362; p < 0.05). The differences of cylindrical powers between healthy and amblyopic eyes were statistically correlated with the difference of logMAR visual acuities of amblyopic and healthy eyes (rho: 0.607; p < 0.01).

Of the amblyopic eyes with myopia, hyperopia and astigmatism, 75%, 42.9%, 33.3%, respectively, were found to have severe amblyopia. The magnitude of cylindrical power was found to be correlated with the age of patients in myopia. (rho: 0.666; p < 0.01) As the spherical powers of amblyopic eyes were increased logMAR visual acuities of amblyopic myopic eyes were increased statistically in myopia. (rho: 0.612; p < 0.01) The differences of spherical equivalents and spherical powers between healthy and amblyopic eyes were statistically correlated with logMAR visual acuity differences of amblyopic eyes and healthy

eyes in myopia respectively (rho: 0.732; p < 0.01; rho: 0.723; p < 0.01).

In hyperopia, spherical powers of amblyopic eyes were statistically correlated with logMAR visual acuities of amblyopic eyes (rho: 0.860; p < 0.01). Also in hyperopia, cylindrical powers of healthy eyes were statistically correlated with cylindrical powers of amblyopic eyes (rho: 0.763; p < 0.01). The differences of spherical powers between healthy and amblyopic eyes were statistically correlated with the differences of logMAR visual acuities of amblyopic eyes and healthy eyes (rho: 0.771; p < 0.01). The statistical results are shown in Table 1.

The inter-ocular visual acuity differences per inter-ocular spherical equivalent differences of the amblyopic eyes were documented as vision per D values for myopia, hyperopia and astigmatism. Refractive disorders of myopia, hyperopia and astigmatism make a mean of 0.081 vision/D, 0.111 vision/D and 0.167 vision/D as follows. In the 0 - 1 D interval the vision per D was 0.881 for hyperopia, 0.812 for astigmatism and 0.343 for myopia. In the 1 - 2 D interval the vision per D was 0.387 for hyperopia, 0.304 for astigmatism and 0.214 for myopia. In the 2 - 3 D interval vision per D was 0.235 for hyperopia, 0.230 for astigmatism and 0.170 for myopia. Vision per D values above 4 D and over were as 0.120 for myopia, 0.118 for hyperopia and 0.105 for astigmatism. The correlation graphs are seen in Figures 1(a)-(d).

4. Discussion

Anisometropia is a disorder of the visual system characterized by decrease in the best corrected visual acuity in one or both eyes with no ocular pathology [1]. According to Woodruff *et al.* [10] the children with anisometropic amblyopia

Table 1. The statistical results.

Correlations in myopia		Correlations in hyperopia		Correlations in astigmatism	
Spearman's rho Correlation Coefficient Sig. (2-tailed) N		Spearman's rho Correlation Coefficient Sig. (2-tailed) N		Spearman's rho Correlation Coefficient Sig. (2-tailed) N	
Age-Amblyopic Eye Cylindrical Power	0.666(**) 0.009 14	Spherical power of amblyopic-LogMAR visual acuity of amblyopic eye	0.860(**) 0.000 16	Amblyopic eye Cylindrical Power-LogMAR visual acuity of amblyopic eye	0.652(**) 0.000 34
Spherical power of amblyopic eye-LogMAR visual acuity of amblyopic eye	0.612(*) 0.020 14	Cylindrical power of healthy eye-Cylindrical power of amblyopic eye	0.763(**) 0.001 16	Spherical equivalent of amblyopic eye-LogMAR visual acuity of amblyopic eye	0.370(*) 0.031 34
Spherical equivalent of amblyopic eye-LogMAR visual acuity of amblyopic eye	0.615(*) 0.019 14	Difference of spherical power between healthy and amblyopic eyes-LogMAR visual acuity of amblyopic eye	0.771(**) 0.000 16	Difference of sqherical equivalents between healthy and amblyopic eyes-LogMAR visual acuity of amblyopic eye	0.362(*) 0.036 34
Difference of sqherical equivalents between healthy and amblyopic eyes-LogMAR visual acuity of amblyopic eye	0.732(**) 0.003 14	-	-	Difference of cylindrical powers between healthy and amblyopic eyes-LogMAR visual acuity of amblyopic eye	0.607(**) 0.000 34
Difference of spherical power between healthy and amblyopic eyes-LogMAR visual acuity of amblyopic eye	0.723(**) 0.003 14	-		-	-

*Correlation is significant at the 0.05 level (2-tailed). **Correlation is significant at the 0.01 level (2-tailed).
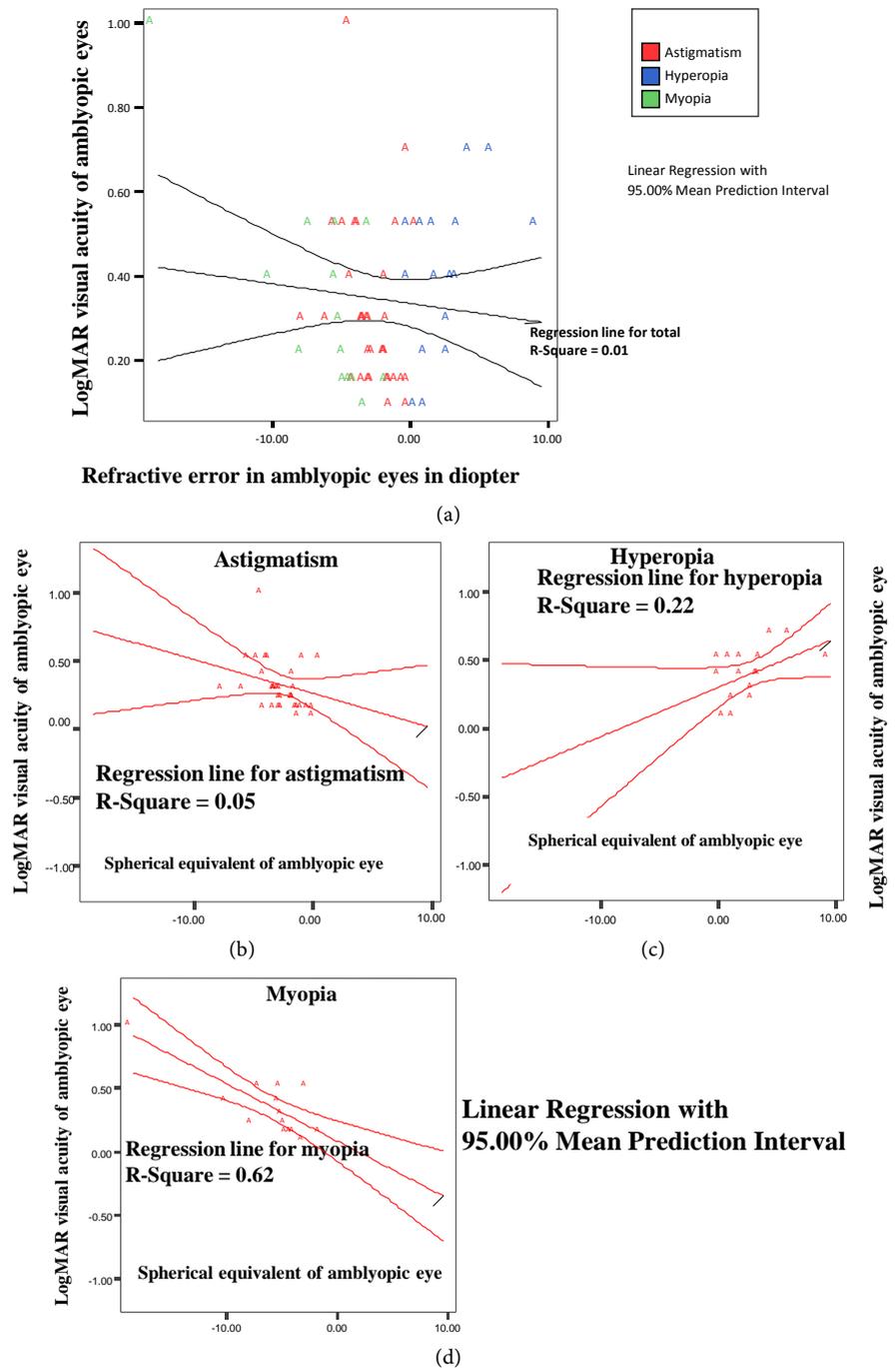
Figure 1. The correlation graphs.

are typically diagnosed later in comparison to other types of amblyopia because they lack of noticeable abnormalities in contrast to children with strabismus who are easily recognized. Anisometropic amblyopic patients apply to the hospital earlier than that of strabismic and mixed amblyopic children. Neither sex nor race affects the age of presentation according to them [10]. In the present study, the mean presentation age of the anisometropic children was 13.7 years old and the median age was 14 years old in the 5 - 18 age group which was even older than the previous studies. Results showed us that our amblyopia detection age

was bigger than that of Woodruff *et al.* [10]. We speculated this to the health care insufficiency of the city, which is in a geographically and socio-economically difficult area.

The cumulative incidence of amblyopia is estimated to be between 2% and 4% in children aged up to 15 years old [3]. We found an incidence of 1% for refractive amblyopia in total patient population. For the age groups 5 to 17 our estimated incidence of anisometropic amblyopia was 1.8%, which seemed similar to the estimated values.

The most important factor in determining the depth of anisometropic amblyopia was thought to be the magnitude of anisometropia. The depth of anisometropia may vary according to the anisometropia magnitude. Ingram and Walker [9] found that patients having astigmatism of +1.50 or more D in either eye were significantly associated with anisometropia. Spherical equivalent of the refractive error of 3.5 dioptres or more, or anisometropia of 1.0 dioptres or more were risk factors for developing amblyopia according to Latvala *et al.* [11]. According to Ingram *et al.* [9] astigmatism of +1.50 or more D in either eye was significantly associated with anisometropia and bilateral hypermetropia of +2.00 or more D and/or +1.50 D or more of astigmatism in either eye was evaluated as abnormal. Kutschke *et al.* [12] informed that patients with anisometropia of myopic and compound astigmatism and mixed astigmatism had poorer visual outcomes. Dolezalova [13] concluded that when the refractory difference was higher than 1 D, there was already a direct relationship between the levels of anisometropia and the depth of amblyopia was particularly marked when the difference was higher than 2 D. In our study, refractive disorder difference of 0.75 D astigmatism between eyes or 1.5 D of underlying spherical refractive disorder difference was enough for developing amblyopia.

Rutstein and Corliss [14] concluded that as the degree of anisometropia increased, the depth of amblyopia became greater. Rutstein and colleagues [14] found that the depth of amblyopia increased along with the increase in hypermetropic anisometropia. Our results in hyperopia showed that the spherical powers of the amblyopic eyes were more strongly correlated with visual acuities than the differences of the spherical powers between amblyopic and healthy eyes. (rho: 0.732; rho: 0.723; p < 0.01). Whereas in myopia, the differences of spherical equivalents and the differences of spherical powers between healthy and amblyopic eyes were more strongly correlated with logMAR visual acuities of the amblyopic eyes compared to spherical powers and spherical equivalents of the amblyopic myopic eyes respectively (rho: 0.732; rho: 0.723; rho: 0.612; rho: 0.615; p < 0.01). In astigmatism, cylindrical power of the amblyopic eye and the difference of cylindrical powers between eyes were more strongly correlated with logMAR visual acuities of the amblyopic eyes than the spherical equivalents and difference of spherical equivalents between eyes in astigmatic amblyopic eyes respectively (rho: 0.652; rho: 0.607; p < 0.001; rho: 0.370; rho: 0.362; p < 0.05). So we can conclude in astigmatic amblyopia that the astigmatic value and the inter-ocular astigmatic value differences are more strongly correlated with amblyopic

visual acuities than astigmatic spherical equivalents. The correlation co-efficients between visual acuities and refractive values were as follows: hyperopia (rho: 0.860; $p < 0.01$); astigmatism (rho: 0.652; $p < 0.01$) and myopia (rho: 0.612; $p < 0.05$). According our results, hyperopia was superior than astigmatism and astigmatism was superior than myopia in amblyopia development. However, refractive disorders of myopia, hyperopia and astigmatism make a mean of 0.081 vision/D, 0.111 vision/D and 0.167 vision/D as follows. According to the mean vision per D values, astigmatism is superior to hyperopia and myopia in amblyopia development.

A meta-analysis by Weale [15] demonstrates that the prevalence of anisometropia in patients without amblyopia increases linearly, approximately 1%, for each 7-year period and its distribution reveals a juvenile rise and a later, post-presbyopic one. A trend for increasing anisometropia with age is also supported by studies of Bourne and colleagues [16]. In our study, we notified that as the age of the patient increased both the spherical and cylindrical values increased statistically in myopia and astigmatism ($p < 0.05$). But such spherical or cylindrical changes were not determined in the hyperopia group. We did not observe the patients for years because it was very difficult. But we analyzed the current data and speculated about it. So we speculated that the hyperopia to be such a factor determined at birth and to be affected much less from environmental factors such as age. However, the astigmatism and the myopia behave like a factor that varies as time goes by.

Bourne and colleagues [16] also notified that against-the-rule astigmatism and oblique astigmatism increased with age. We notified that ATR (67.2%) was the most common astigmatism type seen in amblyopic eyes in the comparison to other types such as WTR (17.2%) and oblique (15.6%). ATR and oblique astigmatism increased with age but it was not statistically significant. However, the age of the myopic patients were statistically correlated with the cylindrical powers of amblyopic myopic patients (rho: 0.666; $p < 0.01$). We observed astigmatism accompanying myopia or hyperopia as a deepening factor for amblyopia depth.

When considered entirely, refractive disorders of myopia, hyperopia and astigmatism make a mean of 0.081 vision/D, 0.111 vision/D and 0.167 vision/D vision per D values according to the spherical equivalent values. So amblyogenic effect of refractive disorder is the biggest in astigmatism, then in hyperopia and then in myopia as follows. In the 0 - 1 D interval the vision per D values showed 0.8 s values for hyperopia and astigmatism and 0.3 s values for myopia. In the 2 - 3 D interval vision per D values showed 0.2 s values which come closer to each other. The vision per D values of refractive disorders were approaching to each other above 4 D of spherical equivalents. The effect of refractive disorder for the development of amblyopia was the greatest for hyperopia and astigmatism compared to myopia between the 0 and 2 D interval and it was decreasing and becoming similar when it became 4 D and over. It seems that the same amount of anisohyperopia and anisoastigmatism leads to deeper amblyopia compared to

the same amount of anisomyopia. Astigmatism seems to have an influence on anisometropic amblyopia more effectively compared to hyperopia and myopia according to the vision per D values. But the vision per D values becomes closer above the 4 D and over values in myopia, hyperopia and astigmatism.

Amblyopia is a common visual disorder and individuals with this condition may experience visual, functional, emotional and social difficulties. Refractive correction alone is often effective and this should represent the first step in evaluating visual acuity of amblyopic eyes. Standard treatment methods may lead to improved visual acuity in most patients. The visual improvement directly attributable to additional therapy (typically patching or atropine) is part of a wider debate that constitutes a clinically significant improvement in visual acuity.

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