Properties of Pediatric Patients with Bilateral Amblyopia

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INTRODUCTION

In children with high refractive errors, isoametropic amblyopia is a rare and dangerous condition in terms of vision (1, 2). Its estimated prevalence is reported in 1 of every 1000 children in a general population with hypermetropia of >5 D (1). It can be easily found among patients with high refractive errors. However, in clinical practice, the diagnosis of amblyopia in children with decreased visual acuity in both eyes due to possible refractive problems, bilateral refractive amblyopia, is not always straightforward. The method for the evaluation of visual acuity and the alertness of the patient are possible confounding factors, but there are patients with a persistent decreased level of visual acuity on repeated examinations, though refractive errors are not usually thought to be compatible with amblyopia. We aimed to study the properties of patients with bilateral refractive amblyopia seen in our pediatric ophthalmology department, including subjects with hypermetropia less and more than 5 D and to analyze any common factors putting these children at special risk for this type of amblyopia.

MATERIALS and METHODS

In the present study, while including patients with bilateral refractive amblyopia, we excluded those with an anisometropia of >1.5 D (sum of spherical and cylindrical equivalents), myopic or hypermetropic refractive defects of >8 D, ocular albinism, previous diagnosis of ocular disease, history of surgery, or the diagnosis of a neurological syndrome or disease.

The study was in compliance with the principles outlined in the Declaration of Helsinki and was approved by the local ethics committee. Informed consent of parents as well as the assent of the children was taken before the enrollment.

All patients underwent a complete ophthalmological examination. Patients with best corrected visual acuity (BCVA) levels below 0.8 OU on the Snellen chart or “E” chart were accepted to have amblyopia. In our patient group, we measured BCVA at the first and last examinations after refraction using trial frames. The eye with the lower level of visual acuity was tested for visual acuity first if one of the eyes was known to have a lower visual acuity. Otherwise, right eye was tested first. We used a test distance of 6 m, and the children’s refractive error was already known by the tester. We accepted the visual acuity value as the line where the patient identified at least 4 letters from 6. In all
patients, the refractive errors were measured 45 min after the last drop of the application of topical cyclopentolate 1% (three times within 5 min intervals) using retinoscopy. The spherical refractive error was partially corrected 1–1.5 D below the spherical error, and the cylindrical error was completely corrected. In all patients, optical correction was used in the follow-up for three months. Occlusion therapy was tried in those with persistent low vision (but a better response was not seen in any of the patients compared with previous optical correction). The achieved value of the best level of visual acuity was determined using a pinhole disc in all patients. Before pupil dilatation, refractive correction by the TNO test was used for stereopsis. The presence and absence of stereopsis was evaluated. The presence of stereopsis was assessed as having stereopsis equivalent to or better than 480 s of arc at the TNO test. The ratio of patients with stereopsis in each group was provided by dividing the number of patients with stereopsis (irrespective of the level) by the total number of patients (with and without stereopsis) in each group.

Statistical Analysis
Best corrected visual acuities (BCVA) of the patients at the initial and final control visits were compared by paired t test. Kruskal–Wallis test was used to compare the groups that were classified on the basis of refractive errors. Chi-square test was used to compare the stereopsis ratios of the groups at the last visit. A two-tailed p<0.05 was considered statistically significant.

RESULTS
In this study, we enrolled 53 patients with bilateral refractive amblyopia with a mean follow-up duration of 2.93±1.59 years (min: 6 months, max: 7 years). The mean age of the patients in the study group was 7.04±2.30 (min: 3, max: 13) years. The distribution of age of the patients is illustrated in Figure 1.

The mean spherical refractive error was +2.98±0.93 D, whereas the mean cylindrical refractive error was +1.28±0.57 D. In total, 32.1% of the patients (n=17) had hypermetropia of 0–4 D, 37.7% (n=21) had hypermetropia of 4–7 D, 22.6% (n=12) had hypermetropia of >7 D, and 5.7% (n=3) had myopic refractive errors >−4 D at the first presentation (Figure 2).

Moreover, 77.4% of the patients (n=41) had a cylindrical refractive error of <2 D, 17% (n=9) had a cylindrical refractive error of 2–4 D, and 5.7% (n=3) had a cylindrical refractive error of >4 D at the first presentation (Figure 3).

Among 17 patients with spherical refractive errors <4 D, 11 (64.7%) had <2 D of astigmatism, while 6 (35.3%) had >2 D of astigmatism.

The BCVA levels of patients with spherical refractive errors of >4 D were not significantly different from those of the patients with
spherical refractive errors of <4 D at the initial evaluation before optical correction for both the right (p=0.94) and left (p=0.18) eyes.

The BCVA levels of patients with spherical refractive errors of >4 D were not significantly different from those of the patients with spherical refractive errors of <4 D at the last control visit after optical correction for both the right (p=0.38) and left (p=0.29) eyes.

However, the ratio of stereopsis levels reached after optical correction were significantly higher in the patients with spherical refractive errors <4 D than those with spherical refractive errors >4 D (p=0.007). The BCVA levels of the patients before and after optical correction are present in Table 1. After the optical correction of refractive error at the final visit, the BCVA levels and stereopsis ratios had a statistically significant rise (p-values for both=0.001).

There was no statistical difference between the predefined refractive groups (<4 D, 4–7 D, >7 D, and >=4 D) when the visual defect detection age (p=0.16) and treatment duration (p=0.48) were considered. Similar to these findings, the visual defect detection age (p=0.16) and treatment duration (p=0.85) do not have statistically significant differences between the different types of refractive errors [hypermetropic, astigmatic, mixed hypermetropic and astigmatic, (the myopic ones were excluded in the Kruskal-Wallis analysis due to their small number)]. There was no deviation in 31 patients (58.5%), while 18 (33%) had esotropia and 4 (7.5%) had exotropia. Among the 31 patients without strabismus, 15 (48.4%) had hypermetropia of ≤4 D, 14 (45.2%) had hypermetropia of >4 D. Moreover, 2 (6.5%) had myopia of >4 D, 21 (67.7%) had cylindrical refractive errors of <2 D, and 10 (32.3%) had cylindrical refractive errors of >2 D.

Among the 22 patients with strabismus, 3 (13.6%) had hypermetropia of ≤4 D, 18 (81.8%) had hypermetropia of >4 D, and 1 (4.5%) had myopia of >4 D. Moreover, 20 (90.9%) patients had cylindrical refractive errors of <2 D and 2 (9.1%) patients had cylindrical refractive errors of >2 D. In total, 31.82% of the patients with strabismus (15 of the 22 patients with strabismus) exhibited an interocular difference in visual acuity at admission as well as 0.8 acuity or worse in both eyes.

**DISCUSSION**

Amblyopia, which is the most common cause of blindness under the age of 45 years, has a prevalence of 3.2% in the general population (2). However, the incidence of isometric amblyopia is 6–26% in patients with hypermetropia, which is a relatively rare condition, than in other types of amblyopia (1-6). Bilateral refractive amblyopia can develop in children with large amounts of uncorrected hypermetropia, astigmatism, or both (3, 4). However, a suspicion of the diagnosis of refractive amblyopia appears in some children with binocular low vision despite somewhat lower levels of hypermetropia. Persistent low vision observed in these patients despite optical correction at subsequent visits influenced us to involve patients with bilateral refractive amblyopia. We aimed to evaluate the clinical properties of these patients together with the patients with isometric amblyopia and analyze any common factors putting these children at special risk for amblyopia.

The shortest follow-up period was 6 months, which was enough for even the oldest patient enrolled in this study as suggested previously (2, 3). The mean age of our patients at admission was 7.04±2.30 (min: 3, max: 13) years. It is reported as 5 years 1 month–5 years 6 months (3, 7, 8) in other studies of patients with isometric amblyopia with hypermetropia of >5 D. The mean sphere measured was also higher in these studies (5.92–6.25 D vs. +2.98±0.93 D in our study) as expected because patients with relatively lower levels of hypermetropia were also enrolled in our study. However, the mean cylindrical refractive error of our patients was +1.28±0.57 D, similar to other studies (1.36 D) (7, 8).

The BCVA level at admission was 0.49 on the Snellen chart. This is higher in comparison with the levels of other studies (0.34–0.35) (7, 8). Increased hypermetropia is reported to be associated with decreased visual acuity (7), no change in visual acuity (5, 8), and increased visual acuity too (9). In our study, treatment with optical correction did not cause any difference in visual acuity between patients with lower (<4 D) and higher levels (>4 D) of hypermetropia. However, the stereopsis ratios were higher in patients with lower levels of hypermetropia (p=0.007). This finding may reflect the effect of high refractive errors on binocular functions. Additionally, the mean age of our patients at diagnosis was relatively high than in other studies. Starting optical correction at an earlier age could have increased the stereopsis ratios in patients with higher refractive errors. This should be studied in future cohort studies starting at an earlier age.

**Table 1. The best corrected visual acuities of patients with bilateral isometric amblyopia at the Snellen chart before and after optical correction**

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<th>Right eye</th>
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<th>Left eye</th>
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<tbody>
<tr>
<td></td>
<td>Before optical correction</td>
<td>After optical correction</td>
<td>p-value</td>
<td>Before optical correction</td>
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<td>p-value</td>
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<tr>
<td>Mean</td>
<td>0.51</td>
<td>0.73</td>
<td>0.001</td>
<td>0.47</td>
<td>0.71</td>
<td>0.001</td>
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<tr>
<td>SD</td>
<td>0.24</td>
<td>0.23</td>
<td></td>
<td>0.22</td>
<td>0.22</td>
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<tr>
<td>Minimum</td>
<td>0.1</td>
<td>0.1</td>
<td></td>
<td>0.1</td>
<td>0.8</td>
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<tr>
<td>Maximum</td>
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<td>0.2</td>
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SD: standard deviation

Strabismus concomitant with bilateral amblyopia has previously been reported in 13–64% of patients (7-9). In our study, 41.5% of the patients had strabismus. Abnormal binocular interaction with suppression may contribute to the development of amblyopia of the non-preferred eye in these patients. Strabismus is also an important factor in the development of amblyopia. Concomitant strabismus probably contributes to amblyopia in addition to the refractive error. Among the 31 patients without strabismus,
15 (48.4%) had hypermetropia of ≤4 D and 14 (45.2%) had hypermetropia of >4D. On the other hand, among the 22 patients with strabismus, 3 (13.6%) had hypermetropia of ≤4 D and 18 (81.8%) had hypermetropia of >4D. As observed, higher refractive errors do not seem to be more prevalent in the patients without strabismus than in those with strabismus. This implies that uncorrected high refractive errors are the primary problem, which in turn led to a break in the ability to maintain motor fusion and hence, the appearance of a manifest deviation. Moreover, the 31.82% of patients with strabismus in our study (15 among the 22 patients with strabismus) exhibited an interocular difference in visual acuity at admission as well as 0.8 acuity or worse in both eyes. Therefore, we also assume that the strabismus itself contributes to the development of amblyopia in patients with strabismus. This question may be answered in further cohort studies starting to follow-up the subjects at earlier ages.

Among the patients with <4 D of hypermetropia, 11 (64.7%) of them had <2 D of cylindrical refractive errors. Therefore, the cause of amlyopia should be answered in these cases. Moreover, the previous refractive error of the patient might not be represented in the refractive status of the patients at the first examination. Therefore, this possible mechanism should be evaluated by prospective cohort studies involving lower age patients in the future. Additionally, the presence of an inability to accommodate normally affecting emmetropization may be another factor for the development of amblyopia in hypermetropic subjects (8). There is a clear necessity to resolve the unknown natural history of amblyopia.

**CONCLUSION**

Lower levels of hypermetropia should be cautiously evaluated as bilateral refractive amblyopia. There is not a significant difference in patients with different types of refractive errors and various levels of hypermetropic errors in terms of the diagnosis age and treatment duration as well as the first and last BCVA levels after treatment using optical correction. However, higher refractive errors are associated with lower stereopsis ratios. Finally, large-scale prospective studies are needed to both confirm and expand the data.

**REFERENCES**

4. Dobson V, Miller JM, Clifford-Donaldson CE, Harvey EM. Associations between anisometropia, amblyopia, and reduced stereoacuity in a school aged population with a high prevalence of astigmatism. Invest Ophthalmol Vis Sci 2008; 49(10): 4427-36. [CrossRef]