Visual parameter status as a predictive factor for the outcomes of occlusion therapy in anisometropic amblyopia

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Abstract:

PURPOSE: The purpose is to compare visual parameters between normal and amblyopic eyes in anisometropic amblyopia and to find predictive factors for occlusion therapy.

METHODS: Sixty patients with anisometropic amblyopia between the ages of 5 and 25 years were enrolled in the prospective, longitudinal, and interventional study. Patients were selected based on no improvement with spectacle correction alone after 1 month of follow-up. Baseline parameters such as LogMAR visual acuity, LEA contrast sensitivity, TNO stereopsis test, online Farnsworth D-15 test for color vision, accommodation with RAF ruler, +2.00/-2.00 flipper test, and dynamic retinoscopy were recorded. All patients were treated with occlusion therapy depending on their grades of amblyopia. After 6 months of follow-up, improvement in visual acuity was recorded with a LogMAR chart and correlated with initial visual parameters. Paired "t" test, Chi-square test, independent "t" test, analysis of variance test were used as statistical analysis.

RESULTS: Visual functions such as contrast sensitivity, accommodative facility, near point of accommodation, and accommodative amplitude showed a statistically significant difference between normal and amblyopic eyes of anisometropic amblyopia patients, whereas color vision did not differ significantly between normal and amblyopic eyes. Sixty-seven percentage of patients had poor stereopsis. Eighty percentage of patients who were younger had improvement in final best-corrected visual acuity and these patients had better stereopsis, contrast sensitivity, and mild-to-moderate amblyopia on initial testing.

CONCLUSION: The age of the patient, degree of anisometropia, spherical equivalent in amblyopic eyes, stereopsis, contrast sensitivity values at initial presentation, and compliance to occlusion therapy were found to be positive predictive factors of occlusion therapy.

Keywords:

Anisometropic amblyopia, contrast sensitivity, occlusion therapy, stereopsis

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Introduction

Amblyopia is one of the most frequent causes of avoidable visual impairment in children.[1] Ophthalmologists must treat amblyopia at a young age and emphasize the value of occlusion therapy to the child's parents because it is challenging to restore binocular single vision (BSV) in amblyopic eyes, especially after a critical age.[2] Only a few studies have attempted to predict the outcomes of occlusion therapy. The aim of the study was to compare the visual characteristics of the normal eye with the amblyopic eye in children diagnosed with anisometropic amblyopia. Variations in visual parameters were utilized to predict visual outcomes following occlusion therapy.

Methods

This prospective, longitudinal, and interventional study was conducted in a Tertiary Eye Care Centre for 18 months. The study followed the principles of the Helsinki Declaration. The Institutional Ethics Committee granted Ethical Approval for the study. Parents and all children were given the information they needed about the study's procedures and goals to give their informed consent.

The study included 60 patients with a diagnosis of anisometropic amblyopia who were younger

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than 25 years old, cognitively capable, and cooperative during testing. Exclusion criteria for the study included patients with other types of amblyopia, anterior or posterior segment diseases, prior amblyopic treatment, and improved visual acuity after spectacle correction alone.

The parents or the patients themselves provided a detailed medical and ocular history. A specific clinical history of past amblyopic and refractive error correction treatments was elicited. All the patients underwent automated refraction, subjective correction, anterior segment examination with the slit lamp, and posterior segment examination with + 90D lens. Visual parameter tests were immediately administered to patients who had previously had their refractive errors corrected. Patients who had cycloplegic refraction and spectacle correction as part of their first refractive error correction were re-evaluated after 1 month to analyze their visual parameters. All visual parameter tests were first performed on the normal eye, followed by the affected eye.

Visual acuity was evaluated at a distance of 4 m using the LogMAR chart. The reading was recorded at 2 m for children who could not read at 4 m, and the values were converted for reading at 4 m. Near vision was evaluated at a distance of 25 cm using a LogMAR near vision chart.

The LEA contrast sensitivity card, which has 25 letters on five cards (five letters on each card), was used for contrast sensitivity testing. The patients were made to read the letters from a distance of 3 m. The distance at which all 25 letters were accurately read was used to calculate the contrast acuity, with a value of 1.25%. Patients who could not read letters at a distance of 3 m were tested at 2 m, and those who could not read them at 2 m were tested at 1 m. Patients were tested at a reading distance (30 cm) if they were still unable to read letters at 1 m. Patients were divided into two groups based on contrast acuity: good (if they could read all 25 letters at a distance of 3 or 2 m) or poor contrast acuity (if they could read all 25 letters at a distance of 1 m or 30 cm).

Accommodative parameters such as accommodative facility (AF), near point of accommodation (NPA), accommodative amplitude (AA), and dynamic retinoscopy were analyzed. Accommodating facility testing was carried out with flippers of +2.00/-2.00 flipper powers; the flipper was flipped until the images appeared clear, and the process was continued for 1 min. It was calculated as cycles/min. NPA and AA were tested using the Royal air force (RAF) ruler and recorded in centimeters and diopters (D), respectively. By using a near target at 30 cm and streak retinoscopy, dynamic retinoscopy was carried out.

The online Farnsworth D-15 color arrangement test (www.color-blindness.com) was used to assess color vision. Patients were asked to arrange randomly-placed colored boxes in the order of changing color hues. Results were analyzed by the software, and values were recorded. The patient wore Armstrong goggles while being examined for stereopsis using TNO charts.

Occlusion therapy was advised following the evaluation of visual characteristics. Depending on their severity of amblyopia, all the patients were advised to wear a large spectacle patch either 4 to 6 h a day or full-time patching. Furthermore, they were advised to engage themselves in near work such as reading, painting, drawing, or playing video games while wearing the patch. Patients were cautioned to use patching therapy while being closely watched by caretakers in order to ensure their safety. The change in visual acuity status was evaluated using LogMAR charts at a distance of 4 m, and the compliance with occlusion therapy was evaluated at the end of the 6-month review visit.

The percentage improvement in visual acuity was calculated using the formula:[3]

$$\frac{\text{Initial visual acuity in affected eye} - \text{final acuity in affected eye}}{\text{Initial visual acuity in affected eye}} \times 100$$

The visual parameters of patients who reported for evaluation at 6 months, including distance visual acuity, near vision, contrast sensitivity, stereopsis, accommodative parameters, and color vision, were analyzed with percentage improvement in visual acuity.

For the purpose of comparison between the amount of refractive error and visual parameters, the spherical equivalent was calculated using the vector blur model,[4]

$$\frac{\sqrt{s^2 + sc + c^2}}{2}$$

where "*s*" refers to spherical power and; "*c*" refers to cylindrical power.

IBM SPSS statistics version 17, Delaware, (Chicago, US), was used to conduct the statistical analysis. The difference in visual parameters between normal and amblyopia eyes was analyzed using a paired *t*-test. The Chi-square test, independent "*t*" test, and Analysis of variances (ANOVAs) were used to identify putative prognostic factors for percentage improvement in visual acuity following occlusion therapy.

Results

The study included 60 patients (28 males and 32 females) with ages ranging from 5 to 25 years. Out of these 60 patients, 26 had myopic or compound myopic astigmatism, 26 had hypermetropic or compound hypermetropic astigmatism and eight had mixed astigmatism. The mean LogMAR best-corrected visual acuity (BCVA) of the normal eyes was 0.04 ± 0.10, while that of the amblyopic eyes was 0.57 ± 0.25; this difference was statistically significant [$P < 0.001$, Table 1]. These patients had statistically significant differences in visual parameters such as contrast sensitivity, NPA, AA, and AF, whereas color vision parameters showed only little difference between amblyopic eyes and normal eyes in these patients [Table 1].

Table 1: Differences in visual parameters between the amblyopic eye and normal eye of patients with anisometropic amblyopia enrolled in the study

Visual parameters ($n=60$)	Amblyopic eye	Normal eye	Paired *t*-test[£]
BCVA	0.57±0.25	0.04±0.10	t (59)=10.75; P<0.001
BCNV	1.53±1.04	0.53±0.04	t (59)=5.25; P<0.001
Contrast sensitivity (number of letters read at 3 m)	8.66±7.16	23.26±4.63	t (59)=−11.15; P<0.001
AF (cycles/min)	8.96±5.81	15.56±3.92	t (59)=−7.81; P<0.001
NPA (cm)	12.68±4.18	11.24±4.88	t (59)=2.18; P<0.003
AA (D)	8.96±3.65	11.86±3.93	t (59)=−3.25; P=0.003
Dynamic retinoscopy (D)	0.31±2.00	1.09±2.69	t (59)=−2.27; P=0.031
Color vision: Angle (°)	18.83±56.32	14.85±60.38	t (59)=0.23; P=0.819
Color vision: TES (°)	18.98±6.76	18.86±5.64	t (59)=0.09; P=0.926
Color vision: S index (°)	1.66±0.52	1.54±0.33	t (59)=1.25; P=0.218
Color vision: C index (°)	1.78±0.63	1.65±0.55	t (59)=1.03; P=0.310

[£]Number in parenthesis refers to DF (calculated as n [60]−1=59). S-index: Selectivity index, C-index: Confusion index, BCVA: Best-corrected visual acuity, BCNV: Best-corrected near vision, TES: Total error score, DF: Degrees of freedom, AF: Accommodative facility, AA: Accommodative amplitude, NPA: Near point of accommodation

According to their stereopsis scores, patients were categorized as having no stereopsis (absence of BSV) in 32 patients, gross stereopsis (capable of identifying the first three plates on TNO cards) in eight patients, fair stereopsis (61°–360°) in 16 patients, and good stereopsis (0°–60°) in four patients. Thus, in the study, 67% of patients with anisometropic amblyopia had impaired stereopsis.

At the 6th month follow-up, only 40 of the 60 patients were presented for reassessment. To determine the favorable prognostic factors for occlusion therapy, all visual parameters of these patients were analyzed with percentage improvement in BCVA. A minimum of 10% improvement in the visual acuity was considered significant (that is, a minimum of one-line improvement in the LogMAR chart).

Only 32 out of 40 review patients had significant improvement in visual acuity. The mean age of 32 patients was 9.75 ± 3.60 years, while the eight patients had a mean age of 14.75 ± 2.21 years. These findings imply that younger patients reacted to occlusion therapy more favorably than older patients, with statistically significant improvement in final BCVA (independent "*t*" test, t = 3.49, [d.f.=38], P = 0.009). The mean spherical equivalent power in these 32 patients was 2.72 ± 1.71 D and in eight patients was 4.62 ± 1.26 D, and this difference was statistically significant (Independent sample "*t*" test, t = 2.48 [d.f.=38]; P = 0.047). These data suggest that the greater the initial spherical equivalent power in the amblyopic eye, the greater the possibility that there would be minimal or no improvement in final BCVA. The mean difference in spherical equivalent power between the normal and the amblyopic eye in these 32 patients was 1.74 ± 0.90 D, whereas the value in these eight patients was 4.43 ± 1.14 D; this difference was found to be statistically significant (Independent "*t*" test, t = 4.37 [d.f.=38]; P = 0.012). These findings suggest that the less the quantum of anisometropia between the normal and amblyopic eyes, the greater the improvement in final BCVA following occlusion therapy.

Out of 32 patients who showed percentage improvement in final BCVA, 24 (75%) patients had good compliance and eight patients (25%) had poor compliance to occlusion therapy; all 8 (100%) patients who did not show percentage improvement in final BCVA had poor compliance with occlusion therapy. This difference was statistically significant (χ^2 [d.f.=1] = 7.5, P = 0.06. However, Yates' correction factor was used because 20% of anticipated frequencies were <5, resulting in Yates χ^2 = 4.7; P = 0.03). According to these findings, a considerably higher percentage of patients who adhered to occlusion therapy had better final BCVA scores than patients who were noncompliant.

According to their 1.25% contrast acuity, the patients were categorized as having good or poor contrast acuity. Out of 40 review patients, 26 patients had good contrast acuity and 14 patients had poor contrast acuity. The mean percentage improvement in final BCVA was 57.34 ± 28.13 and 30.02 ± 28.56 in these 26 and 14 patients, respectively, and this difference approached statistical significance (Independent "*t*" test "*t*" = −2.08, [d.f.=38] P = 0.05). Thus, this result implies that patients with good contrast sensitivity had better outcomes following occlusion therapy.

Out of 32 patients who had improvement in final BCVA following occlusion therapy, BSV was present in 22 patients and absent in 10 patients; out of eight patients who had no improvement in final BCVA, BSV was shown to be present in two patients and absent in six patients. This difference was not statistically significant (χ^2 [d.f.=1] = 2.55, P = 0.110). These results suggest that the presence or absence of BSV may not predict the outcomes of the occlusion therapy in the current study.

Final visual outcomes in relation to grades of stereopsis in these 40 review patients were found to be a significant factor that influences the success of occlusion therapy [Table 2].

The severity of amblyopia in patients was classified as "mild, moderate and severe amblyopia" if the difference in visual acuity between the normal eye and the amblyopic eye was 0.0–0.4, 0.41–0.70, and 0.71–1.00, respectively. Out of 40 patients, 14 had mild amblyopia, 20 had moderate amblyopia, and 6 had severe amblyopia. An improvement in final BCVA was seen in 54.4% of patients with mild amblyopia, 26.6% of patients with moderately severe amblyopia, and 20.5% of patients with severe amblyopia. Thus, the severity of amblyopia appeared to be accompanied by a decrease in the percentage of patients who showed improvement in final BCVA at the review visit; this difference approached statistical significance (One-way ANOVA, P = 0.07).

Table 2: Final visual outcomes in relation to the grade of stereopsis in patients with anisometropic amblyopia who presented for review during the study

Grades of amblyopia	Number of patients	Mean visual acuity in amblyopic eyes before treatment	Mean visual acuity in amblyopic eyes after treatment	Mean percentage improvement in final BCVA	Kruskal–Wallis test
No stereopsis	16	0.67±0.16	0.5±0.26	25.83	*H*=3 (df=3)
Gross stereopsis	8	0.55±0.1	0.46±0.04	15.58	*P*=0.039
Fair stereopsis	14	0.44±0.26	0.19±0.16	57.69	
Good stereopsis	2	0.40	0.00	100.00	

DF: Degrees of freedom, BCVA: Best-corrected visual acuity

The mean AF for these 32 individuals with amblyopia was 8.75 ± 4.57 cycles/min, and for the eight patients whose final BCVA did not improve, it was 9.75 ± 8.01 cycles/min. In amblyopic eyes of 32 patients who showed percentage improvement in final BCVA, the mean NPA and AA were 12.16 ± 3.56 cm and 10.58 ± 3.05 D, respectively, and in amblyopic eyes of eight patients who showed no percentage improvement in final BCVA, the mean values were 21.00 ± 13.31 cm and 6.50 ± 5.00 D, respectively. Statistical analysis could not support these discrepancies. As a result, accommodation-related metrics may not be important prognostic factors affecting the results of occlusion therapy.

On analyzing color vision parameters between amblyopic eyes and normal eyes, it was found that color vision may not predict the outcomes of occlusion therapy in patients with anisometropic amblyopia.

Discussion

Amblyopia is a neuro-developmental disorder of the visual cortex, in which BCVA is decreased due to abnormal experience of visual functions in infancy or early adulthood. This phenomenon is established only in the sensitive period of visual development (that is, from birth to 6–8 years of age).[4] Among all other types of amblyopia, anisometropic amblyopia presents with better visual functions and stereopsis. It has also been proven that in patients with anisometropic amblyopia, visual restoration is possible beyond the critical period of visual development.[5] Thus, in the study, we have included children and young adults up to 25 years of age with anisometropic amblyopia.

Visual parameters of the amblyopic eye of patients with anisometropic amblyopia were extensively analyzed with the contralateral nonamblyopic eye of the same subject serving as control. An attempt was also made to seek putative associations between visual parameters and improvement in final visual acuity in amblyopic eyes undergoing occlusion therapy, in order to identify positive predictive factors of the occlusion therapy.

Previous studies have reported that in amblyopia, visual functions, such as visual acuity, contrast sensitivity, color vision, accommodation, and stereopsis, are significantly affected.[6-8] Similar results were obtained in our study, although significant differences in color vision between normal eyes and amblyopic eyes were not made out.

Levartovsky *et al*.[9] were of the opinion that a poor initial visual acuity and a strabismic type of amblyopia influenced long-term results of successfully-treated amblyopia; however, these investigators classified patients as strabismic, strabismicanisometropic and anisometropic groups, for the purpose of comparison of patients with final visual outcomes. It becomes difficult to compare visual parameters with outcomes of amblyopia treatment when strabismic and anisometropic amblyopia are grouped together, as strabismic amblyopia with poor visual functions may mask the effects of anisometropic amblyopia. Thus, the present study investigated visual parameters and positive predictive factors for occlusion therapy in children with anisometropic amblyopia only.

According to Chen *et al*.,[10] a smaller quantum of anisometropia (<4 D) and initial good visual acuity (LogMAR 0.2–0.6) in the amblyopic eye were associated with a faster resolution of amblyopia. Interestingly, similar results were obtained in the current study; the mean difference in spherical equivalent power between the normal eye and the amblyopic eye in the patients who showed improvement in final BCVA was 1.74 ± 0.90 D, whereas the value in the four patients who showed no improvement in final BVCA was 4.43 ± 1.14 D.

Chatzistefanou *et al*.[11] stated that assessment of the contrast sensitivity function can provide information on visual functions and its influence on occlusion therapy. Our study showed a similar finding; that is, the contrast sensitivity function of amblyopic eyes was significantly subnormal when compared to that of normal eyes. Moreover, patients with good initial 1.25% contrast acuity had better improvement in percentage visual acuity than those who had poor 1.25% contrast acuity.

Levi *et al*.[12] observed that the stereopsis function was better in 56 (67%) of 84 patients with isolated anisometropia; among the 56 patients, 35 patients had good stereopsis (better than 50 arc s). In contrast, in the current study, 67% of patients presented with poor stereopsis, and only 6.8% had good stereopsis (better than 60 arcs). The difference in results obtained was possibly due to the different methods of examination used in the two studies. The "TNO;" cards were used in the current study since they are considered to be foolproof as a result of being devoid of monocular cues; however, they cannot quantify gradual changes in stereopsis. In contrast, "Randot stereotest" used in the study of Levi *et al*.,[12] monocular cues cannot be ruled out, but the test exhibits gradual grading values for evaluating stereopsis.

Singh and Agrawal[13] concluded that grades of amblyopia and accommodative functions were strong predictors for the success of occlusion therapy in individuals with both unilateral and bilateral amblyopia. In the current study, the severity of amblyopia was found to be a predictor of success, although it only approached borderline significance. However, accommodative factors failed to predict successful outcomes following occlusion therapy, possibly due to the use of different methods of testing accommodation. Singh and Agrawal[13] had tested accommodative efforts in their subjects, by adding +3.00 D sphere lens to the distance correction; if one or more lines improvement was noted in near vision, then it was considered "poor accommodative efforts." However, this method becomes unreliable in under-corrected hypermetropic patients or over-corrected myopic patients. In the present study, accommodative parameters such as NPA and AA were evaluated using a universally-accepted method of testing, namely, the "RAF" ruler.

In our study, the age of the patient at presentation and initiation of treatment appeared to influence the outcomes of occlusion therapy. A higher proportion of patients in the younger age group responded well to occlusion therapy. Furthermore, patients who were compliant with occlusion therapy had better visual outcomes when compared to defaulters.

The limitation of the present study was the small sample size. Although 86 children with anisometropic amblyopia were screened, it was possible to include only 60 patients, as it was a challenging task to perform various visual parameters testing in young children, willingness to undergo occlusion therapy and to attend review clinics were not possible with other children.

Conclusion

The young age of the patient, a lower degree of anisometropia between the normal eye and the amblyopic eye, a lower spherical equivalent power in the amblyopic eye, initial good stereopsis and contrast sensitivity, and good compliance to occlusion therapy are possibly positive predictive factors of occlusion therapy. The predictive factors provided in the study will help the treating ophthalmologist to counsel the parents and discuss about the possible outcomes of occlusion therapy accordingly.

The current study highlights the importance of early detection of amblyopia, early intervention with occlusion therapy, and regular follow-up for successful achievement of good visual acuity in the amblyopic eye in patients with anisometropic amblyopia.

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Conflicts of interest

There are no conflicts of interest.

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