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Treatment Outcomes and Clinical Characteristics in Children with Amblyopia at Naresuan University

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Abstract:

Objective: To evaluate the visual outcomes of amblyopia treatment and identify the characteristics of children with newly diagnosed amblyopia.

Material and Methods: This is a retrospective study of children newly diagnosed with amblyopia from January 2016 to December 2019. The assessments consisted of visual acuity (VA) during amblyopia treatment, and treatment effects related to age, gender, type of amblyopia, baseline Logarithm of the Minimum Angle of Resolution visual acuity (LogMAR VA), and treatment compliance. Good outcome was defined as having a best-corrected visual acuity (BCVA) with a ≥2 Snellen line improvement or a ≥20/30 VA (0.17 LogMAR) in the amblyopic eye.

Results: There were 116 amblyopic eyes, corresponding to 89 children, enrolled in the study. The most common cause of the disorder was refractive amblyopia. The mean baseline BCVA was 0.81±0.05 LogMAR. Sixty-four amblyopic eyes (55.2%) had a good treatment outcome, with a mean time for improvement of 13.61±7.89 months. The multivariable analysis in the good outcome group revealed that an age ranging from 5 to 8 years (adjusted odds ratio [aOR]=23.72, 95% confidence interval [CI]: 1.68 to 333.99) and good treatment compliance (aOR=43.09, 95% CI: 2.27-817.97) were more likely to lead to a good outcome.

Conclusion: Amblyopia has the potential to improve with early treatment and good compliance. Early detection and increased care may be necessary in patients who are non-compliant in order to achieve the best possible therapeutic outcome.

Keywords: amblyopia, factors, treatment, visual outcome

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Introduction

Amblyopia is a developmental cortical disorder of the visual pathway that is primarily caused by abnormal visual stimuli. It is defined as a unilateral or bilateral decrease in best-corrected visual acuity (BCVA) that cannot be attributed to any structural abnormality of the eye. It is associated with abnormal visual experience. Amblyopia is frequently caused by strabismus, anisometropia, or high bilateral refractive error, as well as visual deprivation during a critical period of visual development in infancy or early childhood.[1] Estimates of prevalence vary between 1.0% to 3.0% depending on the population studied and the definition used.[2-5]

When amblyopia is detected and treated early, the complete or partial reversal of amblyopia-induced visual acuity loss is possible. However, it is difficult to compare success rates and predictors of treatment outcome across studies due to differences in disease distribution, study design, treatment regimens, and definitions of success. Numerous studies have reported success rates ranging between 43.8% and 81.0%.[6-10]

The aim of this study was to determine the visual outcomes of amblyopia treatment and the effects of age, gender, type of amblyopia, baseline Logarithm of the Minimum Angle of Resolution visual acuity (LogMAR VA), and treatment compliance on visual outcome.

Material and Methods

The Naresuan University Institutional Review Board approved the study protocol. The medical records of 89 children, who were newly diagnosed with amblyopia between January 2016 and December 2019 at Naresuan University Hospital's Department of Ophthalmology were retrospectively reviewed.

To be included in the study, the children had to be literate, aged 3-18 years, newly diagnosed with amblyopia at the time of the first visit, able to perform the Snellen visual acuity test, and to have had at least one year of follow-up. Children were excluded if they had medical conditions or ocular diseases associated with a decreased visual acuity. The children's demographic data comprised their age, gender, type of amblyopia, treatment regimens, baseline LogMAR BCVA, and treatment compliance. BCVA was assessed on the first consultation, every one to three months after treatment, and at the last follow-up appointment. The result of the visual acuity test was converted to LogMAR units.[11]

Amblyopia was defined as unilateral when there at least two lines of difference on the Snellen BCVA test between the eyes and as bilateral when the Snellen BCVA test result of each eye was less than 20/40.[1] The following subtypes of amblyopia were classified: 1. strabismic amblyopia – manifested deviation in distance and/or near fixation with or without glasses; 2. refractive amblyopia: a. anisometropia – greater than 1.50 diopters (D) of hyperopia, 2.00 D of astigmatism, and 3.00 D of myopia, and b. isoametropia – 4.00–5.00 D or more of hyperopia, 5.00–6.00 D of myopia, and 2.00–3.00 D of astigmatism; 3. deprivative amblyopia – a known or documented cause of sensory deprivation; and 4. combined-mechanism amblyopia – presence of more than one amblyogenic factor.[1,12]

The severity of amblyopia was classified as mild/moderate when the BCVA was between 20/40 and 20/80 (0.3-0.6 LogMAR) and severe when the BCVA was between 20/100 and 20/400 (0.7-1.3 LogMAR). Treatment was provided in accordance with the American Academy of Ophthalmology's Preferred Practice Pattern.[1]

Definition of treatment compliance:

Compliance to patching was classified as "good" if it was >80.0%, "fair" if it was between 80.0% and 50.0%, and "poor" if it was <50.0% of the prescribed time. The compliance percentage was calculated by dividing the number of actual patching hours per month by the patching hours per month prescribed by the ophthalmologist.

$$\frac{\text{Hours of actual patching per month}}{\text{Hours of prescribed patching per month}} \times 100\%$$

Compliance to glasses was classified as "good" if worn daily, "fair" if worn ≥3 days per week, and "poor" if worn <3 days per week. Compliance to combined treatment was classified as "good" if compliance to both patching and glasses was good, "fair" if compliance to either patching or glasses was fair, and "poor" if compliance to either patching or glasses was poor.

The amblyopic eyes were categorized into two groups: 1) good outcome group and 2) poor outcome group. Good outcome was defined as a BCVA of ≥20/30 (0.17 LogMAR) or a change of ≥Snellen lines from the baseline.[6,7]

Proportions were expressed as percentages, and the chi-square test was used to determine proportional differences. Student's t-test was used to analyze continuous variables, which were shown as mean ±standard deviation (SD). Mixed-effects multivariable logistic regression analyses were performed to determine the risk factors associated with good visual outcome. The level of significance was set at a p-value of <0.050. The Stata Statistical Software Release 12 was used to carry out the statistical analysis (StataCorp LP, College Station, TX, USA).

Results

A total of 89 children (116 amblyopic eyes) were recruited in the study. Each child had a minimum follow-up period of one year and a maximum period of 4 years. Twenty-seven children had bilateral amblyopia. The clinical characteristics of the participants are summarized in Table 1.

With ages ranging between 3 and 18, the mean age of the 89 patients (116 amblyopic eyes) at the first consultation was 7.78±3.53 years, and the majority was females. The mean BCVA at baseline was 0.81±0.05 LogMAR. In a decreasing order, the most common causes of amblyopia were related to the refractive type [isoametropia (41.1%, n=48) and anisometropia (16.4%, n=19)], strabismus (25.0%, n=29), the combined-mechanism type (15.5%, n=18), and deprivation (1.7%, n=2). Among the isoametropia cases, the refractive error was most frequently associated with the astigmatism+myopia combination. In the majority of anisometropic children, the refractive error was due to hyperopia. Almost all patients with strabismic amblyopia exhibited esotropia. Half of the amblyopic eyes were classified as severe amblyopia. Overall, 51.7% of the samples (n=60) reported good compliance. Good prescription glasses compliance (81.5%) was significantly higher than compliance to patching (24.2%) and combined treatment (27.6%).

Table 1 Clinical characteristics

Characteristics (n=116)	Value
Gender, n (%)	
Male	35 (30.2)
Female	81 (69.8)
Age, mean (SD) (years)	7.78±3.53
Type of amblyopia, n (%)	
Isoametropia	48 (41.1)
Anisometropia	19 (16.4)
Strabismia	29 (25.0)
Deprivation	2 (1.7)
Combined-mechanism	18 (15.5)
Baseline LogMAR VA, mean (S.D.)	0.81±0.05
Severity of amblyopia, n (%)	
Mild-moderate	58 (50.0)
Severe	58 (50.0)
Treatment, n (%)	
Glasses	54 (46.5)
Patching	33 (28.5)
Combination therapy	29 (25.0)
Compliance, n (%)	
Good	60 (51.7)
Fair	25 (21.6)
Poor	31 (26.7)

S.D.=standard deviation, LogMAR VA=Logarithm of the Minimum Angle of Resolution visual acuity

The differences in clinical characteristics between patients with good outcome and those with poor outcome are shown in Table 2. Children who experienced a good outcome were younger than children with poor outcome (mean age of 6.9 years vs. 8.87 years, respectively), and they also had a higher rate of good compliance (67.2% vs. 32.7%, p-value≤0.001). The baseline LogMAR VA in children with isoametropia in the good outcome group was considerably worse than that of their counterparts in the poor outcome group (0.87 vs. 0.53, p-value=0.027). No significant correlation between the type of amblyopia and visual outcome was observed (p-value=0.099).

A good outcome was noted in 55.2% (n=64, 95% CI: 45.66 to 64.41) of amblyopic eyes. Isoametropia was the most frequently occurring condition among the improving eyes. The mean time required to improvement was 13.61±7.89 months (range 3-48 months). Good compliance was found to be higher among patients with improving amblyopic eyes (n=64) compared to fair and poor compliance (67.2% vs. 32.8%, p-value≤0.001). Thirty (46.9%) improving eyes continued to show a LogMAR VA of <0.3 with a mean improvement time of 15.90±6.09 months (range 3-34 months). The mean BCVA of the good and poor outcome groups during the last follow-up appointment was 0.36±0.04 and 0.82±0.06 LogMAR, respectively.

Table 2 Differences in clinical characteristics between good and poor outcome groups

Characteristics	Good outcome (n=64)	Poor outcome (n=52)	p-value
Female gender, n (%)	45 (70.3)	36 (69.2)	0.900[a]
Age, mean (S.D.) (years)	6.90±3.02	8.87±3.83	0.003[b]*
Type of amblyopia, n (%)			0.099[a]
Isoametropia	31 (48.5)	17 (32.7)	
Anisometropia	13 (20.3)	6 (11.5)	
Strabismus	13 (20.3)	16 (30.8)	
Deprivation	1 (1.6)	1 (1.9)	
Combined-mechanism	6 (9.3)	12 (23.1)	
Baseline LogMAR VA, mean (S.D.)			
Isoametropia	0.87±0.10	0.53±0.04	0.027[b]*
Anisometropia	0.70±0.09	0.86±0.19	0.387[b]
Strabismus	0.97±0.17	0.73±0.08	0.188[b]
Deprivation	0.7	2.28	NA
Combined-mechanism	1.15±0.17	0.84±0.16	0.242[b]
Severity of amblyopia, n (%)			0.709[a]
Mild-moderate	31 (48.4)	27 (51.9)	
Severe	33 (51.6)	25 (48.1)	
Treatment, n (%)			0.174[a]
Glasses	34 (53.1)	20 (38.5)	
Patching	14 (21.9)	19 (36.5)	
Combination therapy	16 (25.0)	13 (25.0)	
Compliance, n (%)			<0.001[a]*
Good	43 (67.2)	17 (32.7)	
Fair	15 (23.4)	10 (19.2)	
Poor	6 (9.4)	25 (48.1)	

[a]Chi square test, [b]Student's t-test, *significant p-value<0.050, S.D.=standard deviation, LogMAR VA=Logarithm of the Minimum Angle of Resolution visual acuity

The univariate analysis showed that the ages of <5 years (odds ratio [OR]=25.66, 95% CI: 1.51 to 436.00) and 5–8 years (OR=24.18, 95% CI: 2.30 to 253.85) were associated with a higher likelihood of having a good outcome than ages >8 years. Moreover, good compliance was more likely to lead to a good treatment outcome than fair or poor compliance (OR=12.98, 95% CI: 2.03 to 82.82). There was no evidence that the kind of amblyopia was a significant predictor of outcome (Table 3).

The multivariable analysis revealed that an age of 5–8 years (adjusted odds ratio [aOR]=23.72, 95% CI: 1.68 to 333.99) and good compliance (aOR=43.09, 95% CI: 2.27–817.97) were statistically significant predictors of a favorable outcome (Table 4).

Table 3 Univariate analysis of factors associated with good outcome

Characteristics	OR	95% CI	p-value
Sex (ref.=male)			
Female	1.30	0.31–5.43	0.716
Age (years) (ref.>8)			
<5	25.66	1.51–436.00	0.025*
5–8	24.18	2.30–253.85	0.008*
Baseline LogMAR VA	2.43	0.63–9.37	0.195
Type of amblyopia (ref.=combined-mechanism)			
Isoametropia	8.77	0.99–77.80	0.051
Anisometropia	11.50	0.94–140.13	0.056
Strabismus	2.29	0.29–17.81	0.430
Deprivation	3.25	0.03–409.37	0.633
Severity of amblyopia (ref.=mild-moderate)			
Severe	1.33	0.37–4.69	0.662
Treatment (ref.=combination therapy)			
Glasses	1.73	0.35–8.55	0.503
Patching	0.42	0.08–2.25	0.311
Compliance (ref.=fair and poor)			
Good	12.98	2.03–82.82	0.007*

Ref.=reference, LogMAR VA=Logarithm of the Minimum Angle of Resolution visual acuity, OR=odds ratio, CI=confidence interval

Table 4 Multivariable analysis of factors influencing good outcome

Characteristics	aOR	95% CI	p-value
Sex (ref.=male)			
Female	1.60	0.24–10.76	0.626
Age (years) (ref.>8)			
<5	5.43	0.18–165.98	0.332
5–8	23.72	1.68–333.99	0.019*
Baseline LogMAR VA	9.13	0.85–98.42	0.068
Treatment (ref.=combination therapy)			
Glasses	0.16	0.01–2.24	0.173
Patching	0.36	0.04–3.14	0.354
Compliance (ref.=fair and poor)			
Good	43.09	2.27–817.97	0.012*

Ref.=reference, LogMAR VA=Logarithm of the Minimum Angle of Resolution visual acuity, aOR=adjusted odds ratio, CI=confidence interval

Discussion

Treatment for amblyopia has a success rate of 43.8% to 81.0%.[6–10] In this study, 55.2% of amblyopic eyes achieved a good outcome. The mean time to improvement was month 13, indicating that this pediatric patient population requires extended treatment and follow-up lasting beyond 12 months. The relatively low rate of a positive outcome in this study sample suggests that some children were followed for a shorter period of time (at least one year); thus, their the treatment they received did not have the adequate duration for it to yield an improvement in clinical outcome.

The Pediatric Eye Disease Investigator Group discovered that when children aged 3 to 10 years old were treated with refractive correction alone for mild isoametropic amblyopia associated with high hyperopia (≥4.00 D) and/or astigmatism (≥2.00 D), 74.0% of them achieved a binocular VA of 20/25 or better, and some children continued to show VA improvement for up to a year post-treatment.[13] Lin PW et al. reported on visual outcomes following spectacle treatment in children with bilateral high refractive amblyopia; they found that visual acuity improved to 0.0 LogMAR at 18 months.[14] Hessa et al. examined the efficacy of amblyopia treatment in anisometropia and discovered that the time required to achieve resolution is more than one year.[15]

In this study, 30 (46.9%) of the improved eyes had a LogMAR VA of 0.3, and the mean time to improvement was 16 months. Literature suggests that, with continued treatment, VA can improve even further. It follows, therefore, that patients with poor compliance to treatment protocols require additional time to achieve an optimal outcome. However, follow-up visits vary according to compliance and caregiver. As a result, determining the precise time improvement is achieved is challenging.

The mean age at presentation was 7.78±3.53 years. This is due to one of the inclusion criteria, which required the children to be able to read the Snellen chart. This study demonstrated that children treated earlier in life had a higher success rate, which is consistent finding with those of previous research.[7,16,17] According to the univariate analysis, amblyopia was found to be more receptive to treatment in younger age groups (children <5 and 5–8 years of age). However, the multivariable analysis revealed that only the children in the 5–8 years age group were more responsive to treatment. However, the small number of children under the age of five included in this study sample could have been a factor leading to such a finding. Nevertheless, this result is consistent with Holmes et al.'s finding that children in the younger age groups (ages between 3 and 7 years) were more responsive to treatment for moderate and severe amblyopia than those in the older age groups (ages between 7 and 13 years).[16] Although the average response to treatment is smaller among children over the age of 8, some studies have demonstrated a significant response to treatment in this age group.[18,19] Al-Mahdi H. and Bener A. examined children with strabismic amblyopia from the age of six to twelve years of age and discovered that age had no effect on visual outcome.[9]

Although children with worse VA have a greater potential for visual improvement[17], some studies have suggested that a worse initial VA is commonly predictive of a poor visual outcome.[6,7,20] However, this research found no correlation between baseline LogMAR VA and visual outcome.

Consistent with the outcomes of this study, previous literature has demonstrated that refractive amblyopia is more prevalent than strabismic or sensory amblyopia.[5–7,10] Chia et al. reported that the most common refractive error was astigmatism, including anisometropia and isoametropia[5]; however, this study discovered that isoametropic myopia, astigmatism as well as anisometropic hyperopia were also prevalent.

Children with anisometropic amblyopia had the best visual outcomes, while those with pure strabismic amblyopia experienced moderate level outcomes, and those with

combined-type amblyopia were associated with poorer outcomes.[21] Earlier investigations have reported that the type of anisometropia was significantly associated with visual acuity improvement in amblyopic eyes.[15] However, no significant difference was found between the types of amblyopia and visual outcome in this study.

Compliance to treatment was found to be a significant factor for visual outcome. This finding corroborates the results reported by previous research, which have identified an association between poor compliance to therapy and poor outcomes.[6,22] Children treated with patching or a combination of both patching and glasses had a lower compliance rate than children treated exclusively with glasses; this could be attributed to the possibility of a lower resistance to wearing glasses on the part of children receiving treatment for amblyopia.

This study had a low rate of good patching compliance (24.2%) compared to an earlier study that reported compliance rates ranging from 49.0% to 87.0%.[23] However, the reasons for non- compliance were not explored in this research. Santos et al. reported a remarkable rate of patching compliance, which they attributed to the use of a patching diary.[7] Patching can be distressing for both the child and parents, which could have a negative effect on compliance.[24,25] Another significant issue with patching is the visual impact of wearing the patch. Furthermore, the physical properties of the patch may contribute to poorer compliance.[25] Adherence to patching therapy is one of the vital factors in achieving better visual outcomes, and it is influenced by a variety of considerations. A better understanding of these influencing factor could result in a more favorable treatment outcome.

The findings of this research are subject to at least four limitations. First, it is retrospective in nature, wherein follow-up visits were spaced variably and not uniformly across all children, unlike what would be the case in a prospective study. Second, the long-term stability of visual acuity following treatment improvement or discontinuation was not evaluated. Third, since compliance was determined based on caregiver recall, the correlation detected between visual outcome and compliance is at least presumably unreliable. Finally, each subtype of amblyopia was not evaluated due to the small sample size. Thus, future research should be prospective in nature and employ a larger sample size for each subtype of amblyopia as well as a longer follow-up period.

Conclusion

Early treatment and good compliance were found to be significant predictors of a favorable outcome. This underscores the importance of eye health education and screening to determine the need for amblyopia treatment. Noncompliance is the primary cause of treatment failure, but the underlying causes of noncompliance are not well-understood. Hence, it is critical to conduct additional research to ascertain the root causes of poor compliance. Emphasis on educational and motivational intervention is warranted to ensure that both caregivers and children understand the importance of compliance to prescribed therapy.

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Faculty of Medicine, Naresuan University.

Conflict of interest

None

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