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Efficacy of Full Refractive Correction as a Primary Treatment for Anisometropic Amblyopia in Children Aged 5 to 15 Years: A Longitudinal Cohort Study

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ABSTRACT

Purpose: To evaluate the visual outcomes of full refractive correction as a standalone initial treatment for anisometropic amblyopia in children aged 5 to 15 years and to identify predictive factors for treatment success. **Methods:** This longitudinal cohort study included 128 children (mean age 9.8 ± 3.2 years) with previously untreated anisometropic amblyopia. All participants received full-time spectacle correction based on their full cycloplegic refraction. The primary outcome measure was the improvement in best-corrected visual acuity (BCVA) in the amblyopic eye, measured in LogMAR units. Treatment was considered successful if the inter-ocular acuity difference was reduced to 0.2 LogMAR units (2 lines) or less. Follow-up examinations were conducted at 3, 6, 12, and 24 months. **Results:** After 12 months, 78 of 128 participants (60.9%) achieved successful visual outcomes with spectacle correction alone. The mean BCVA in the amblyopic eyes improved significantly from a baseline of 0.78 ± 0.25 LogMAR to 0.35 ± 0.21 LogMAR. Children in the younger cohort (5 to <10 years) demonstrated a higher success rate (71.2%) compared to the older cohort (10 to 15 years) (48.3%, $p < 0.01$). Logistic regression analysis identified the initial degree of anisometropia as the strongest predictor of treatment failure, with each additional diopter of anisometropia increasing the odds of an unsuccessful outcome. The type of refractive error (myopic vs. hyperopic) was not found to be a statistically significant predictor. **Conclusion:** Full refractive correction serves as an effective primary intervention for a majority of children with anisometropic amblyopia, including those up to 15 years of age. While younger age is associated with better outcomes, substantial visual improvement can still be achieved in older children. The initial magnitude of anisometropia is a critical factor for prognosticating treatment success and may help identify patients who will likely require earlier adjunctive therapy, such as occlusion or atropine penalization.

KEYWORDS: Anisometropic Amblyopia, Refractive Correction, Visual Acuity, Spectacle Treatment, Pediatric Ophthalmology, Neuronal Plasticity, Visual Outcome.

INTRODUCTION

Defining the Scope of Amblyopia

Amblyopia, often termed "lazy eye," represents a neurodevelopmental disorder of the visual system characterized by a unilateral, or less commonly bilateral, reduction in best-corrected visual acuity (BCVA) that cannot be attributed to any structural abnormality of the eye or posterior visual pathways [1]. It is the most common cause of monocular vision loss in children, affecting an estimated 2-4% of the population [5]. The underlying mechanism is rooted in abnormal visual experience during the critical period of visual development, typically from birth to around 7-8 years of age. During this period, the brain's visual cortex learns to process inputs from both eyes to create a single, high-resolution, three-dimensional image. If the input from one eye is consistently blurred, misaligned, or obstructed, the cortical neurons responsible for processing information from that eye fail to develop properly, leading to a functional suppression of that eye's pathway by the brain [3].

The clinical significance of amblyopia extends far beyond the simple loss of acuity in one eye. The condition impairs binocular vision, stereopsis (depth perception), and contrast sensitivity, which can have lifelong implications for educational attainment, career choices, and overall quality of life [4]. Furthermore, individuals with amblyopia are at a significantly increased lifetime risk of severe vision loss, as an injury or disease affecting their "good" eye can result in bilateral visual impairment. Given its prevalence and

potential for long-term morbidity, the timely and effective treatment of amblyopia remains a cornerstone of pediatric ophthalmology.

Anisometropic Amblyopia: The Challenge of Unequal Focus

Amblyopia can be classified based on its underlying cause, with the most common forms being strabismic (due to ocular misalignment), deprivational (due to obstruction of the visual axis, e.g., congenital cataract), and anisometropic. Anisometropic amblyopia, the focus of this study, arises from a significant difference in refractive error between the two eyes. This discrepancy results in one eye being in sharper focus than the other. The brain, receiving one clear image and one consistently blurred image, preferentially develops the neural pathways associated with the clearer eye while suppressing the input from the more out-of-focus, or ametropic, eye [9].

Unlike strabismic amblyopia, which often presents with a visible eye turn, anisometropic amblyopia is frequently asymptomatic and can go undetected until a child undergoes vision screening at school or a routine eye examination [5]. The absence of overt signs makes early detection challenging, and many children are diagnosed at an older age, potentially outside the traditionally defined critical period for visual development. The degree of anisometropia required to induce amblyopia varies, but differences of greater than 1.50 to 2.00 diopters (D) of hyperopia or astigmatism, or greater than 3.00 D of myopia, are generally considered high-risk [9].

Current Treatment Paradigms and Existing Gaps

The foundational principle of amblyopia treatment is to first provide a clear retinal image in both eyes and then to encourage the brain to use the amblyopic eye. For anisometropic amblyopia, the first and most crucial step is full-time spectacle wear to correct the underlying refractive error. This optical correction alone can, in many cases, lead to a significant improvement or complete resolution of the amblyopia, as it provides the brain with two clear images for the first time, potentially stimulating the underdeveloped neural pathways [7].

However, for cases where spectacle correction alone is insufficient, the standard of care involves adjunctive therapies designed to penalize the dominant, non-amblyopic eye, thereby forcing the brain to rely on the amblyopic eye. The most common methods are occlusion therapy (patching the good eye for a prescribed number of hours per day) and pharmacological penalization (using atropine eye drops to blur the vision in the good eye) [10]. While effective, these treatments are often associated with significant psychosocial challenges, including poor compliance due to discomfort and social stigma, emotional distress for both the child and parents, and, in rare cases, the induction of reverse amblyopia in the treated eye [8].

Despite the established efficacy of these treatment modalities, a critical gap exists in the literature regarding the full potential of spectacle correction as a standalone therapy, particularly in older children. Most major clinical trials, such as those conducted by the Pediatric Eye Disease Investigator Group (PEDIG), have focused primarily on children under the age of 10, with many specifically targeting those under 7 years [6, 10]. There is a prevailing clinical assumption that neuronal plasticity diminishes significantly after this age, rendering treatments less effective. Consequently, there is a lack of robust, longitudinal data on the outcomes of spectacle correction alone in children aged 10 to 15 years. Furthermore, while factors like the initial depth of amblyopia and age are known to influence outcomes [8], a more granular understanding of which specific patient characteristics predict success or failure with optical correction alone could enable clinicians to develop more personalized and efficient treatment strategies.

Study Rationale and Objectives

The management of anisometropic amblyopia in older children and young adolescents presents a clinical dilemma. Is it beneficial to trial a period of spectacle correction alone, or should more aggressive adjunctive therapy be initiated immediately? A prolonged period of ineffective optical treatment could waste valuable time when neuronal plasticity, though reduced, may still be present. Conversely, prematurely escalating treatment to patching or atropine places an unnecessary burden on patients who might have improved with spectacles alone.

This study was therefore designed to address this critical knowledge gap. The primary objective was to longitudinally evaluate the efficacy of full refractive correction as the sole initial intervention for anisometropic amblyopia in a broad cohort of children aged 5 to 15 years. A secondary objective was to identify baseline demographic and clinical factors, including age, the initial degree of anisometropia, and the type of refractive error, that are associated with the final visual outcome. By providing a detailed analysis of treatment response in this understudied older population, we aim to offer evidence-based guidance for clinicians in prognosticating outcomes and optimizing management strategies for this common and treatable form of childhood vision loss.

METHODS

Study Design and Setting

This study was conducted as a longitudinal, prospective cohort study at two tertiary pediatric ophthalmology centers. Data were collected from all eligible patients presenting between January 2020 and December 2022, with a subsequent follow-up period extending to 24 months. The study protocol was approved by the Institutional Review Boards of both participating centers and adhered to the tenets of the Declaration of Helsinki. Informed consent was obtained from a parent or legal guardian of each participant, and assent was obtained from children aged 10 years and older.

Participant Selection

Participants were recruited from patients referred to the pediatric ophthalmology clinics for routine eye examinations or failed vision screenings. The inclusion and exclusion criteria were designed to create a homogenous cohort of children with previously untreated anisometropic amblyopia.

Inclusion Criteria:

1. Age between 5 and 15 years at the time of diagnosis.
2. Presence of anisometropia meeting the following criteria: ≥1.50 D spherical equivalent difference for hyperopia, ≥3.00 D spherical equivalent difference for myopia, or ≥1.50 D difference in cylindrical power.
3. Presence of amblyopia, defined as an inter-ocular difference in BCVA of at least 0.2 LogMAR units (equivalent to two lines on a standard acuity chart).
4. No prior history of amblyopia treatment, including spectacle wear, patching, or atropine therapy.
5. Absence of strabismus greater than 8 prism diopters at distance or near fixation, as determined by prism and alternate cover testing.

Exclusion Criteria:

1. Presence of any ocular pathology (e.g., congenital cataract, glaucoma, optic nerve hypoplasia, retinal disease) that could independently affect visual acuity.
2. Known systemic or neurological conditions associated with visual impairment (e.g., cerebral palsy, Down syndrome).
3. Previous intraocular surgery.
4. Deprivational or strabismic amblyopia as the primary diagnosis.
5. Inability to cooperate with visual acuity testing or other required examination procedures.

Baseline Examination and Intervention

Upon enrollment, each participant underwent a comprehensive ophthalmic examination performed by a fellowship-trained pediatric ophthalmologist. The examination included:

- **Visual Acuity:** BCVA was measured for each eye separately using a standardized protocol with full refractive correction in place. Early Treatment Diabetic Retinopathy Study (ETDRS) LogMAR charts were used at a distance of 4 meters. For younger children unable to identify letters, Lea Symbols or HOTV charts were employed. Testing was conducted using a surround-crowding protocol to accurately reflect the functional visual acuity in amblyopia.
- **Cycloplegic Refraction:** To determine the full refractive error and eliminate the influence of accommodation, cycloplegia was induced using two drops of 1% cyclopentolate hydrochloride administered five minutes apart. A third drop was instilled if pupillary reaction to light was still present after 30 minutes. Retinoscopy was performed 45-60 minutes after the first drop to obtain an objective measure of the refractive error.
- **Ocular Motility and Alignment:** A detailed sensorimotor examination was performed, including cover-uncover and prism and alternate cover tests at distance and near, to rule out significant strabismus. Ocular versions and ductions were assessed to ensure full motility.
- **Slit-Lamp and Fundus Examination:** The anterior segment was examined to rule out media opacities, and a dilated fundus examination was performed to confirm the absence of any structural abnormalities of the retina or optic nerve.

Following the baseline examination, all participants were prescribed spectacles that provided the full cycloplegic refractive correction for both eyes. Families were extensively counseled on the critical importance of full-time spectacle wear (defined as all waking hours except during bathing or contact sports).

Follow-up Protocol and Outcome Measures

Participants were scheduled for follow-up visits at 3, 6, 12, and 24 months after the initial prescription of spectacles. At each follow-up visit, the full comprehensive examination, including measurement of BCVA and a cycloplegic refraction, was repeated. Compliance with spectacle wear was assessed at each visit through structured interviews with both the parent and the child. Participants reporting less than 75% wear time were noted, but were retained in the analysis based on an intention-to-treat principle.

The **primary outcome measure** was the improvement in BCVA in the amblyopic eye from baseline to the 12-month follow-up visit.

The **secondary outcome measure** was the resolution of amblyopia at 12 months, defined as a final inter-ocular BCVA

difference of ≤0.2 LogMAR units. Participants meeting this criterion were classified as having a "successful" treatment outcome. Those with a persistent inter-ocular acuity difference >0.2 LogMAR were classified as having an "unsuccessful" outcome with spectacle correction alone and were subsequently offered adjunctive therapy per standard clinical practice.

Baseline variables collected for analysis as potential predictors of outcome included age at diagnosis, gender, initial BCVA in the amblyopic eye, magnitude of anisometropia (in spherical equivalent), and type of refractive error (categorized as myopic anisometropia or hyperopic anisometropia).

Statistical Analysis

All data were entered into a secure database and analyzed using SPSS version 26.0 (IBM Corp., Armonk, NY). Descriptive statistics (mean, standard deviation, percentages) were used to summarize the demographic and clinical characteristics of the cohort. The change in BCVA from baseline to 12 months was assessed using a paired t-test.

To identify factors associated with treatment success, participants were dichotomized into "successful" and "unsuccessful" outcome groups based on the secondary outcome measure. The cohort was also stratified into two age groups for comparative analysis: a younger group (5 to <10 years) and an older group (10 to 15 years). Chi-square tests were used to compare success rates between these two age groups and between different types of refractive error. An independent samples t-test was used to compare the mean initial degree of anisometropia and baseline BCVA between the successful and unsuccessful groups.

Finally, a multivariate logistic regression analysis was performed to identify independent predictors of a successful outcome. Variables that showed a trend towards significance ($p < 0.10$) in the univariate analyses were included in the regression model. A p-value of <0.05 was considered statistically significant for all analyses.

RESULTS

Participant Demographics and Baseline Characteristics

A total of 145 children were initially assessed for eligibility. Of these, 17 were excluded (8 had coexisting strabismus greater than 8 prism diopters, 4 had previously worn spectacles, 3 had underlying ocular pathology, and 2 were unable to complete reliable acuity testing). This resulted in a final study cohort of 128 participants who were followed for at least 12 months. Ten participants were lost to follow-up before the 24-month visit but were included in the primary 12-month analysis.

The cohort comprised 68 males (53.1%) and 60 females (46.9%). The mean age at the time of diagnosis was 9.8 years (SD ± 3.2 years; range, 5.1 to 14.9 years). The younger age group (5 to <10 years) included 73 participants, and the older age group (10 to 15 years) included 55 participants.

At baseline, the mean BCVA in the amblyopic eye was 0.78 ± 0.25 LogMAR (approximately 20/120 Snellen equivalent), and the mean BCVA in the fellow (non-amblyopic) eye was 0.05 ± 0.08 LogMAR (approximately 20/20 Snellen equivalent). The mean degree of anisometropia, calculated as the absolute difference in spherical equivalent between the two eyes, was 3.15 ± 1.45 D. Hyperopic anisometropia was present in 82 participants (64.1%), while myopic anisometropia was present in 46 participants (35.9%). There were no statistically significant differences in baseline characteristics between the younger and older age groups.

Primary Outcome: Improvement in Visual Acuity

After 12 months of full-time spectacle wear, a statistically significant improvement in visual acuity was observed in the amblyopic eyes of the overall cohort. The mean BCVA improved from 0.78 ± 0.25 LogMAR at baseline to 0.35 ± 0.21 LogMAR at the 12-month follow-up ($p < 0.001$, paired t-test). This represents a mean improvement of 0.43 LogMAR, which is equivalent to gaining over four lines of acuity on a standard eye chart. The majority of this improvement occurred within the first 6 months of treatment, with the mean BCVA at that time point being 0.41 ± 0.23 LogMAR.

Secondary Outcome: Resolution of Amblyopia

Based on the predefined criterion for success (an inter-ocular acuity difference of ≤0.2 LogMAR), 78 of the 128 participants (60.9%) were classified as having a successful outcome with spectacle correction alone at the 12-month mark. The remaining 50 participants (39.1%) were classified as having an unsuccessful outcome and were subsequently recommended for adjunctive therapy.

A significant difference in success rate was observed between the two age groups. In the younger cohort (5 to <10 years), 52 of 73 participants (71.2%) achieved a successful outcome. In contrast, only 26 of 55 participants (47.3%) in the older cohort (10 to 15 years) met the success criterion. This difference was statistically significant ($\chi^2 = 7.82$, $p = 0.005$). Despite the lower success rate in the older group, it is noteworthy that nearly half of these children still responded favorably to optical correction alone.

Factors Predicting Treatment Outcome

Univariate analyses were performed to compare the baseline characteristics of the "successful" and "unsuccessful" treatment groups. The successful group had a significantly younger mean age (8.9 ± 2.8 years vs. 11.1 ± 3.3 years, $p < 0.001$) and a significantly lower mean degree of initial anisometropia (2.65 ± 1.10 D vs. 3.95 ± 1.60 D, $p < 0.001$). There was no significant difference in baseline BCVA or gender distribution between the two outcome groups. When comparing refractive error types, the success rate for myopic anisometropia (67.4%) was slightly higher than for hyperopic anisometropia (57.3%), but this difference did not reach statistical significance ($p = 0.24$).

The multivariate logistic regression analysis confirmed these findings. After controlling for other variables, both younger age and a lower initial degree of anisometropia remained independent and significant predictors of a successful treatment outcome. The analysis revealed that for each one-year increase in age, the odds of treatment success decreased by approximately 18%. More strikingly, for each one-diopter increase in the magnitude of anisometropia, the odds of a successful outcome with spectacles alone decreased by 45% (Odds Ratio = 0.55; 95% Confidence Interval: 0.41-0.74; $p < 0.001$). This identifies the initial degree of refractive disparity between the eyes as the most powerful prognostic factor.

DISCUSSION

Summary and Interpretation of Key Findings

This study provides compelling evidence that full refractive correction, when used as a primary, standalone intervention, is a highly effective treatment for a substantial proportion of children with anisometropic amblyopia across a wide age range of 5 to 15 years. The principal finding is that approximately 61% of children in our cohort achieved resolution of their amblyopia within 12 months of simply wearing their prescribed glasses full-time. This result underscores the fundamental importance of optical correction as the foundational, and often sufficient, step in the management of this condition [1].

The observed mean improvement of over four LogMAR lines in the amblyopic eye is not only statistically significant but also represents a profound clinical benefit that can impact a child's functional vision and quality of life. Our results align with and extend the findings of previous studies, such as that by Chen et al. [7], which reported significant improvement with spectacle correction alone in a younger cohort. However, by including children up to 15 years of age, our study challenges the conventional therapeutic pessimism often associated with treating amblyopia in older age groups. The finding that nearly half (47.3%) of the children aged 10-15 achieved a successful outcome is particularly noteworthy. It suggests that meaningful neuronal plasticity persists well into early adolescence, and that these patients should not be denied a trial of the simplest, least burdensome therapy.

Furthermore, our analysis identified two critical prognostic factors: age at treatment initiation and the initial magnitude of anisometropia. The inverse relationship between age and treatment success is well-established [8, 10], and our data reinforce this principle. However, the identification of the degree of anisometropia as the single strongest predictor of outcome offers significant clinical utility. This finding suggests that a child with a high degree of anisometropia (e.g., >4.00 D) has a much lower probability of resolving their amblyopia with spectacles alone, irrespective of their age. This information can be used to manage patient and parental expectations and may justify an earlier introduction of adjunctive therapies like patching in high-risk cases to maximize the potential for visual rehabilitation.

Contextualizing Results within the Literature

The success rate observed in our study is comparable to those reported in other investigations focusing on optical correction. The PEDIG group, in a study of 3 to <7-year-old children, found that vision improved with spectacles alone in about one-third of subjects, with many more showing some improvement [6]. Our higher overall success rate of 61% may be attributable to our slightly different success criterion or demographic variations. Stewart et al. [8] also emphasized that a significant portion of visual recovery often occurs after optical correction is provided, before any occlusion therapy is even initiated. Our study contributes to this body of literature by providing robust longitudinal data for a broader and older age cohort, which has been a notable gap.

The discussion surrounding the "critical period" for visual development has been evolving. While traditionally thought to end around age 7 or 8, numerous studies now support the concept of a period of "residual plasticity" that extends beyond this window [10]. The PEDIG trial on treating amblyopia in older children (7 to 12 years) demonstrated that even patching could yield significant visual gains [10]. Our findings regarding spectacle correction complement this work, suggesting that providing a clear retinal image can itself trigger this residual plasticity, even without the need for penalization of the fellow eye. The success in our 10-15 year old cohort provides a strong argument against therapeutic nihilism in teenagers and advocates for an initial trial of optical correction in all previously untreated patients.

Our finding that the magnitude of anisometropia is a powerful predictor is also consistent with clinical intuition and previous research. Afsari et al. [9] demonstrated a strong association between the prevalence of amblyopia and the degree of anisometropia in preschool children. It is logical to infer that a larger discrepancy in refractive error

creates a more profound and entrenched pattern of cortical suppression, making it more resistant to reversal by optical means alone. Our study quantifies this relationship, providing a valuable tool for clinical prognostication.

Clinical Implications and Recommendations

The results of this study have several direct implications for clinical practice:

1. **Spectacle Correction as a Universal First Step:** Our findings strongly advocate for a mandatory trial period of full-time spectacle wear for at least 3 to 6 months in all children diagnosed with untreated anisometropic amblyopia between the ages of 5 and 15. The majority of improvement in our cohort was seen by the 6-month mark, making this a reasonable timeframe to assess efficacy before considering treatment escalation.
2. **Informed Prognostication:** Clinicians can use the initial degree of anisometropia to provide more accurate prognostic information to families. For a child with mild to moderate anisometropia (<3.00 D), the prognosis with glasses alone is very good. For a child with high anisometropia (>4.00 D), parents should be counseled from the outset that spectacles are a crucial first step but that adjunctive therapy like patching will very likely be necessary.
3. **Optimism in Treating Older Children:** The significant improvement seen in the 10-15 year old cohort should encourage clinicians to actively treat, rather than simply monitor, amblyopia in this age group. A positive and proactive approach, starting with spectacle correction, is warranted and evidence-based.
4. **Reducing Treatment Burden:** By demonstrating the high efficacy of spectacle-only treatment, our study supports a management approach that can spare a majority of children from the psychosocial and practical burdens associated with patching and atropine therapy [2, 3]. This patient-centered approach prioritizes the simplest, least invasive intervention first.

Strengths and Limitations

This study has several strengths, including its prospective, longitudinal design, the use of a standardized examination and visual acuity testing protocol, and the inclusion of a broad and clinically relevant age range. By focusing exclusively on previously untreated patients, we were able to isolate the effect of the primary intervention without confounding factors.

However, certain limitations must be acknowledged. First, the study was not a randomized controlled trial; we lacked a control group that did not receive treatment or one that received immediate adjunctive therapy. Second, compliance with spectacle wear was assessed via self-report, which may be subject to recall bias. While we counseled families extensively, variations in actual wear time could have influenced the outcomes. Third, our cohort was recruited from tertiary care centers, which may introduce a selection bias towards more severe or complex cases, potentially underestimating the true success rate in a general population. Finally, while we followed patients for up to 24 months, longer-term data would be beneficial to assess the stability of the visual gains and to monitor for any regression.

Future Research Directions

This study opens several avenues for future investigation. A randomized controlled trial comparing a strategy of initial spectacle correction versus immediate full-time patching in older children (e.g., 10-15 years) with severe anisometropic amblyopia would be valuable to determine the most efficient treatment protocol for this high-risk group. Additionally, research incorporating objective measures of binocular function and stereopsis would provide a more complete picture of the functional recovery beyond just visual acuity. Finally, employing advanced neuroimaging techniques, such as functional MRI or visual evoked potentials, could help elucidate the neural mechanisms underlying the recovery of vision in older children, providing biological insight into the nature of extended cortical plasticity.

CONCLUSION

In conclusion, this study demonstrates that full refractive correction is a powerful and effective primary treatment for anisometropic amblyopia in children aged 5 to 15 years. It leads to significant visual improvement in the majority of patients, reinforcing its role as the essential foundation of amblyopia management. While treatment outcomes are moderated by age, a substantial number of older children and young adolescents can achieve amblyopia resolution without the need for more demanding adjunctive therapies. The initial magnitude of anisometropia emerges as the most critical predictor of success, offering clinicians a valuable tool for risk stratification and the formulation of individualized treatment plans. These findings advocate for a patient-centered, stepwise approach that prioritizes optical correction in all cases, thereby optimizing visual outcomes while minimizing the burden of treatment.

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