



Refractive Accommodative Esotropia Treated by Asymmetric Refractive Accommodative Esotropia Correction

Zhisheng Li

Department of Ophthalmology
Beijing Radiant Children's Hospital, Beijing, China
Visual Brain Functional Imaging Joint Research Laboratory
Radiant-Peking University Magnetic Resonance Imaging Research Center
Peking University, Beijing, China

Geng Li

Radiant Children's Hospital Management Group, Hong Kong
Visual Brain Functional Imaging Joint Research Laboratory
Radiant-Peking University Magnetic Resonance Imaging Research Center
Peking University, Beijing, China

Xueqiang Li

Department of Ophthalmology
Beijing Radiant Children's Hospital, Beijing, China

Na Xue

Department of Ophthalmology
Beijing Radiant Children's Hospital, Beijing, China

Lianjun Sun

Department of Ophthalmology, Shenyang Radiant Children's Hospital
Shenyang, Liaoning, China

Huifang Zheng

Radiant Youth Vision Rehabilitation Center
Third People's Hospital of Xinjiang Autonomous Region
Urumqi, Xinjiang Uygur Autonomous Region, China

Lavonne Rayer Lee

Department of Ophthalmology
Beijing Radiant Children's Hospital, Beijing, China
Radiant Children's Hospital Management Group, Hong Kong

Diana Danlai Fung

Department of Ophthalmology, Beijing Radiant Children's Hospital, Beijing, China
Visual Brain Functional Imaging Joint Research Laboratory
Radiant-Peking University Magnetic Resonance Imaging Research Center
Peking University, Beijing, China

ABSTRACT

To compare deviation improvement in children with residual refractive accommodative esotropia after previous treatment with spectacles, part-time patching and visual training with asymmetric refractive accommodative esotropia correction vs. full hyperopic correction. 72 participants (F=34, mean age 5.81 years) with residual partially refractive accommodative esotropia, mean deviation without glasses was 18.33 ± 5.61 prism dioptres (PD) at distance and 22.64 ± 5.82 PD at near. Participants (mean baseline visual acuity 62.43 ± 18.97 letters) were randomly assigned to treatment for 24-months with asymmetric refractive accommodative esotropia correction (n=36) or full hyperopic correction (n=36). Change in deviation, visual acuity, refraction and anisometropia from baseline to the 24-month assessed by a masked examiner until deviation resolved and visual acuity stabilized. At 24 months, mean deviation with glasses improved from baseline by 21 PD with asymmetric esotropia correction, by 7 PD with full hyperopic correction at near vision. Mean visual acuity was improved from baseline 72.08 ± 16.62 letters to 108.06 ± 2.47 letters; refraction was decreased from baseline 5.03 ± 2.75 dioptres (D) to 2.49 ± 1.39 D in refractive accommodative esotropia eye (EE) in asymmetric refractive accommodative esotropia correction group, Visual acuity difference between EE and dominated eye (DE) was reduced from baseline 3.22 ± 3.39 to 0.25 ± 0.44 . Anisometropia was improved from the baseline 1.65 ± 1.78 D to 0.14 ± 0.14 D. Overall treatment outcome was not related to age, sex, or prior treatment history, but were related to better baseline deviation and visual acuity. **Conclusion:** Deviation and visual acuity were greater improvement with asymmetric esotropia correction than full hyperopic correction treatment at 24-month in children with residual refractive accommodative esotropia.

Keywords: Residual refractive accommodative esotropia; asymmetric anisometropic correction; hyperopic correction; visual acuity, angle of deviation.

INTRODUCTION

Refractive accommodative esotropia is one of the most common forms of childhood eye misalignment[1-5]. Children with refractive esotropia are typically hyperopic. The treatment refractive accommodative esotropia consists the prescription of eyeglasses according to degree of hyperopia and amblyopia to correct the children's refractive error (full hyperopic correction), and surgical correction for cases with the esotropia which is significantly under corrected despite full hyperopic correction[6]. This study assessed the efficacy of asymmetric refractive accommodative esotropia correction vs. full hyperopic correction for residual refractive accommodative esotropia.

MATERIALS AND METHODS

The study was supported by the Asia Pediatric Ophthalmologist Association and was conducted by the Radiant Children's Hospital Group. Protocol and HIPAA compliance informed consent forms were approved by the ethics committee of Radiant Children's Hospital (Beijing, China). The parent or guardian of each patient provided written informed consent. The study was overseen by an independent data and safety monitoring committee. Patients were randomly assigned to asymmetric refractive accommodative esotropia correction as treatment groups or to full hyperopic correction as control groups. Patients had esotropia corrected to 10 prism diopters (PD) of orthotropia at both distance and near vision with use of full cycloplegic hyperopic correction as the diagnosis of refractive accommodative esotropia[5]. Exclusion

criteria included deteriorative accommodative esodeviation, history of developmental delay, and any form of neurologic impairment.

Patients

The 72 participants (F=34, 47.2%) with residual refractive accommodative esotropia were aged 4 to 10 years (mean age 5.64 ± 1.94 in treated; 5.81 ± 1.39 in control) with a history of full correction of the cycloplegic refractive error treatment (100% spectacle wear at least 1 years; 90% patching 4 hours per day at least 1 months; 20% atropine at least 0.28 years and 100% visual training such as visual perception, spatial localization, hand eye coordination in both groups) at least 1.5 years in Table 1.

Prior to enrollment into the study, participants were examined and excluded for potential ocular pathological defects. Full orthoptic and ophthalmic examinations were performed including intraocular pressure measurements, fundus examinations, stereopsis, visual contrast, cycloplegic refraction, visual electrophysiology and binocular single vision, where cooperation was adequate. Binocular sensory testing was performed through the patient's optimum hyperopic correction. Cycloplegia was performed with one drop of 1% cyclopentolate and 1% tropicamide, repeated in five to ten minutes, with retinoscopy performed after 60 minutes. At each visit, visual acuity and binocular vision were assessed without cycloplegia, by an individual masked to the treatment assignment. Corrective lenses were prescribed based on deviation, refraction, accommodation and subjective trials of lenses according to the prescription principle: asymmetric hyperopic esotropia correction by increasing plus power of spectacles in DEs and decreasing plus power of spectacles in EEs to maintain high accommodation and to reduce esotropia[7-9]. All participants were prescribed new glasses at the initial appointment. The control group was prescribed the full hyperopic correction. The corneal light reflex test, cover-uncover test and alternated cover test were used to assess the participants' ocular alignment. The baseline demographics and the history at enrollment are listed in Table 1. All participants maintained a calendar on which treatments were logged. Calendars were reviewed at each follow-up visits. After randomization, follow-up visits were scheduled at the 40th day (± 2 days), the 3-month (± 1 week), 6-month (± 1 week), 12-month (± 1 week) and 24-month (± 1 month).

Asymmetric refractive accommodative esotropia correction methods

In the asymmetric refractive accommodative esotropia correction group, all participants were instructed to wear spectacles for all waking hours. Corrective lenses for refractive accommodative esotropia were prescribed based on their deviation and refraction with cycloplegia at the enrollment. In this groups, if the visual acuity of the fellow eye reached 0 logMAR, no refraction correction was prescribed for that eye. When the visual acuity difference between two eyes larger than 300 D, the brain is difficult to fuse, and it may inhibit the visual acuity of one eye, so if both esotropia and hyperopic were fully corrected, the visual acuity difference between two eyes would be increased. The prescription principle of asymmetric refractive accommodative esotropia correction is to increase plus power of spectacles in DEs and to decrease plus power of spectacles in EEs, in order to blur the DE, decrease the degree of esotropia and stimulate accommodation in the EE[8]. At the second visit (the 40th day), if the refractive errors of the EE were improved to +5.00 D without cycloplegia (cycloplegia can cause a transient hyperopia, frequently cycloplegia can make the lens being shorter which would damage the hyperopic eye), the corrective lens was prescribed at +4.50 D to reduce the plus

further if the patient can accommodate. Participants were asked to return at the 40th day, 3, 6, 12, and 24-month, respectively for each follow-up therapy including the deviation, the visual acuity, and the accommodative ability test and prescribed new corrective lens accordingly at each follow-up visiting. The recurrence induced by poor eye coordination as well as the developed diplopia would be prevented by the asymmetric refractive accommodative esotropia correction.

Investigators and patients were unmasked to the asymmetric refractive accommodative esotropia correction group, but responders and non-responders were based on the deviation and visual acuity which were assessed by an individual masked to the treatment assignment. In the asymmetric refractive accommodative exotropia correction group, both exotropia and hyperopia were fully corrected or symmetrically under corrected by no more than 0.83 PD for distance vision with glasses and 1.50 D.

Randomization

Each patient was randomly assigned with an equal probability to either asymmetric refractive accommodative esotropia correction as the treatment group or to full hyperopic correction as the control group. Randomization was accomplished following data entry by clinical staff using a permuted design of varying block sizes, with a separate sequence of computer-generated random numbers for each clinical site. Both children and parents were masked.

Statistical Analyses

The sample size of 80 participants was computed to have 90% power with 2-sided type I error rate of 5% and type II error of 10%, the cure rate assumes 45% in the asymmetric refractive accommodative esotropia correction group and 15% in the full hyperopic correction group, a 5% loss to follow-up rate, a minimum sample size of 40 patients in each group was planned.

The primary outcome was the change of the deviation and visual acuity scores in EEs from baseline to 40 day (± 2 days). A modified intent-to-treat analysis of covariance was performed to estimate the treatment group difference in mean change in deviation and visual acuity at 40 day and a 2-sided 95% confidence interval (CI), adjusted for baseline deviation and visual acuity. For each patient, the difference in mean deviation, visual acuity, interocular acuity difference, refractive errors and degree of anisometropia with 95% confidence intervals were computed at the 40th day, 3, 6, 12 and 24-month. Latency and amplitude of visual electrophysiology were computed at the 24-month.

The resolution of esotropia was defined when the deviation in the EE was no more 6 PD. The proportion of patients whose esotropia resolved was computed and 95% confidence intervals were calculated. The association of age, sex, prior treatment history (spectacles, patching, atropine and visual training), binocular vision, visual acuity, degree of anisometropia with improvements in the resolution of esotropia and treatment days were assessed using the analysis of linear regression, paired test and one sample test. All p-values were two-tailed. SPSS version 22 was used for data analyses.

RESULTS

Baseline Characteristics

Between April 2017 and May 2020, 72 participants (F=34) with residual refractive partially accommodative esotropia, the mean deviation without glasses was 21.88 ± 7.42 PD for distance vision and 23.47 ± 7.63 PD for near vision. mean baseline visual acuity of 62.43 ± 18.97 letters; mean baseline interocular acuity difference of 3.29 ± 2.97 lines. The baseline demographics, clinical history and characteristics of the study cohort are provided in Tables 1.

Treatment and follow-up

After the first visit, 4 patients were dropped in both groups, respectively. The 40th day primary outcome, the subsequent 3-month, 6-month, 12-month and 24-month visits were completed by 36 (90%) participants in both groups, respectively (Fig.1). The deviation and visual acuity measurement were performed by masked testers at 90% of visits for both groups. No participant in both groups was prescribed treatment other than the randomly assigned treatment during the study.

Binocular vision in EE

At the 40th day primary outcome visit, after adjusting for baseline, mean difference of deviation at near with glasses drastically improved from baseline by 1 PD (95% CI: 0.4 to 1.8 PD) with asymmetric refractive accommodative esotropia correction, and by 0.1 PD (95% CI: -0.1 to 0.4 PD) with full hyperopic correction (Table 2). Follow-up at the 3, 6, 12 and 24 months, mean difference of deviation at near glasses by 7 PD (95% CI: 6.5 to 8.2 PD), 11 PD (95% CI: 10.4 to 12.3 PD), 16 PD (95% CI: 14.7 to 17.2 PD), 21 PD (95% CI: 20.1 to 22.6 PD), respectively, with asymmetric refractive accommodative esotropia correction, and by 5 PD (95% CI: 4.0 to 5.2 PD), 6 PD (95% CI: 5.4 to 7.1 PD), 9 PD (95% CI: 7.7 to 9.8 PD), 13 PD (95% CI: 12.0 to 14.1 PD), respectively, with full hyperopic correction. At the 40th day primary outcome visit, after adjusting for baseline, mean difference of deviation at far with glasses improved from baseline by 2 PD (95% CI: 1.0 to 2.9 PD) with asymmetric refractive accommodative esotropia correction, and by 1 PD (95% CI: 0.4 to 1.8 PD) with full hyperopic correction. Follow-up at the 3, 6, 12 and 24 months, mean difference of deviation at far with glasses by 8 PD (95% CI: 6.7 to 8.8 PD), 10 PD (95% CI: 8.8 to 11.5 PD), 12 PD (95% CI: 10.2 to 13.1 PD), 18 PD (95% CI: 16.1 to 19.2 PD), respectively, with asymmetric refractive accommodative esotropia correction, and by 5 PD (95% CI: 3.9 to 5.5 PD), 7 PD (95% CI: 5.9 to 7.7 PD), 10 PD (95% CI: 8.7 to 10.5 PD), 13 PD (95% CI: 12.1 to 14.0 PD), respectively, with full hyperopic correction. In both asymmetric refractive accommodative esotropia correction and full hyperopic correction groups, the deviations were improved gradually ($p < 0.05$) in 24 months, but there were not statistically significant different ($t = 1.00$, $p = 0.324$) in the deviation between the 1st day and the 40th day visits in full hyperopic correction groups only. From the 3-month visit to the 24-month visit, there were a statistically significant difference ($t = 2.97$, $p < 0.005$ for 3-month visit; $t = 3.57$, $p < 0.001$ for 6-month visit; $t = 4.65$, $p < 0.001$ for 12-month visit; $t = 5.62$, $p < 0.001$ for 24-month visit) in the deviations at far with glasses between asymmetric refractive accommodative esotropia correction and full hyperopic correction groups. From the 6-month visit to the 24-month visit, there were a statistically significant difference ($t = 4.16$, $p < 0.001$ for 6-month visit; $t = 5.90$, $p < 0.001$ for 12-month visit; $t = 6.26$, $p < 0.001$ for 24-month visit) in the deviations at near with glasses between asymmetric refractive accommodative esotropia correction and full hyperopic correction groups (Table 2).

Visual acuity in EE

At the 40th day primary outcome visit, after adjusting for baseline, mean difference of visual acuity improved from baseline by 19 letters (95% CI: 15.4 to 22.9 letters) with asymmetric refractive accommodative esotropia correction, and by 0 letters with full hyperopic correction. Follow-up at the 3, 6, 12 and 24 months, mean difference of visual acuity improved from baseline by 26 letters (95% CI: 21.3 to 30.6 letters), 30 letters (2-sided 95% CI: 25.6 to 35.2 letters), 34 letters (95% CI: 29.1 to 39.1 letters), 36 letters (95% CI: 30.5 to 41.4 letters) with asymmetric refractive accommodative esotropia correction, and 1 letters (95% CI: 0.4 to 1.8 letters), 3 letters (95% CI: 1.3 to 3.8 letters), 4 letters (95% CI: 2.0 to 4.9 letters), 8 letters (95% CI: 5.8 to 9.5 letters) with full hyperopic correction, respectively (Table 3).

Interocular acuity difference in EE

With asymmetric refractive accommodative esotropia correction, mean difference of interocular acuity difference reduced from baseline by 2.3 lines (95% CI: 1.4 to 3.3 lines) at the 40th day, by 2.6 (95% CI: 1.5 to 3.6 lines) at 3-month, by 2.8 lines (95% CI: 1.8 to 3.9 lines) at the 6-month, by 2.9 (95% CI: 1.9 to 4.0 lines) at 12-month, by 3.1 lines (95% CI: 2.0 to 4.2 lines) at the 24-month. In the hyperopic correction treatment group, mean difference of interocular acuity difference reduced from baseline by 1.7 lines (95% CI: 1.0 to 2.5 lines) at the 40th day, by 1.7 lines (95% CI: 1.7 to 2.5 lines) at 3-month, by 1.7 lines (95% CI: 0.9 to 2.5 lines) at the 6-month, by 1.6 lines (95% CI: 0.8 to 2.4 lines) at 12-month, by 1.4 lines (95% CI: 0.6 to 2.2 lines) at the 24-month. The interocular acuity differences were reduced gradually in both groups, but it was reduced faster and more in the asymmetric refractive accommodative esotropia correction group. Compared with the hyperopic correction group, the interocular acuity difference was reduced 2.3 lines more (95% CI: 1.4 to 3.3 lines) in the asymmetric refractive accommodative esotropia correction group at the 40th day, 2.6 lines more (95% CI: 1.5 to 3.6 lines) at 3-month, 2.8 lines more (95% CI: 1.8 to 3.9 lines) at the 6-month, 2.9 lines more (95% CI: 1.9 to 4.0 lines) at 12-month, 3.1 lines more (95% CI: 2.0 to 4.2 lines) at the 24-month (Table 3).

Improvement lines of acuity in EE

In asymmetric refractive accommodative esotropia correction group, improvement lines from baseline to best measure acuity was dramatically increased by 4 lines (95% CI: 3.2 to 4.8 lines) at the 40th day, by 5 lines (95% CI: 4.2 to 6.1 lines) at the 3-month, by 6 lines (95% CI: 4.9 to 6.8 lines) at the 6-month, by 6 lines (95% CI: 5.4 to 7.5 lines) at the 12-month, and by 6 lines (95% CI: 4.7 to 7.2 lines) at the 24-month (Table 3).

Anisometropia in EE

With the asymmetric refractive accommodative esotropia correction, the degree of anisometropia without cycloplegic refraction decreased (Table 3). Mean difference of the degree of anisometropia reduced from baseline by 0.8 D (95% CI: 0.5 to 1.1 D) at the 40th day, by 1.0 D (95% CI: 0.6 to 1.4 D) at the 3-month, by 1.3 D (95% CI: 0.9 to 1.7 D) at the 6-month, by 1.4 D (95% CI: 0.9 to 1.8 D) at the 12-month, and by 1.5 D (95% CI: 0.1 to 2.0 D) at the 24-month (Table 3).

Visual electrophysiology in EE

For the latency (LP) and amplitude (AP) of visual electrophysiology, statistically significant differences in AP100 ($P < 0.01$) and LP100 ($P < 0.01$) between patients with the asymmetric

refractive accommodative esotropia correction vs. the full hyperopic correction were found (Fig. 1 and Fig. 2). The reduction of LP 100 and raise of AP100 were observed in the asymmetric refractive accommodative esotropia correction group.

Treatment outcome was not related to age, sex, or prior treatment history, but were related to better baseline binocular vision and visual acuity.

DISCUSSION

Children with refractive accommodative esotropia display asymmetrical anisometropia [1, 3-5, 10, 11]. When the visual acuity difference between the two eyes reaches a certain level, the normal accommodation will be reduced. Eyes is difficult to focuses on things, the visual acuity of one eye will be inhibited, and the stereoscopic vision will be lost. The asymmetric refractive accommodative esotropia correction increase the plus power of the spectacles in dominated eyes and reduce the plus power of the spectacles in refractive accommodative exotropia eyes to reduce the visual acuity difference between two eyes, let the brain make eyes focused on things, create a power for asymmetric accommodation and restore the stereoscopic vision [7-9]. This study evaluated the efficacy of asymmetric refractive accommodative esotropia correction vs. full hyperopic correction for residual refractive accommodative esotropia.

The patients with accommodative esotropia wore correcting lenses early in life, some of them do not require treatment as adults, but many of them do not end with childhood and do not develop stable binocular single vision [3, 12]. Full correction of hyperopic refractive error might hinder emmetropization process in children [11, 13-15]. On the other hand, refractive correction of hyperopia might improve the accuracy of accommodation [16, 17]. The optimal amount of correction and threshold for hyperopic correction varied among publications [18, 19]. In this study of 72 participants (mean age 5.73 ± 1.67) with residual refractive partially accommodative esotropia, we found that mean difference of deviation at both near and distance visions with glasses drastically improved with the asymmetric refractive accommodative esotropia correction, especially at the 24-months from baseline by 21 PD (95% CI: 20.1 to 22.6 PD) at near, and by 18 PD (95% CI: 16.1 to 19.2 PD) at distance. The improvement in the deviations were initiated from the 40th day to the 24-months gradually. Mean difference of visual acuity improved from baseline by 19 letters (95% CI: 15.4 to 22.9 letters) at the 40th day and 36 letters (95% CI: 30.5 to 41.4 letters) at the 24-month with the asymmetric refractive accommodative esotropia correction. Mean difference of interocular acuity difference reduced from baseline by 2.3 lines (95% CI: 1.4 to 3.3 lines) at the 40th day and by 3.1 lines (95% CI: 2.0 to 4.2 lines) at the 24-month. Mean difference of the degree of anisometropia reduced from baseline by 1.5 D (95% CI: 0.1 to 2.0 D) at the 24-month. The results of our study support the asymmetric refractive accommodative esotropia correction dramatically improved deviation, visual acuity, interocular acuity and anisometropia among children with refractive accommodative esotropia throughout the later years of emmetropization up to 10 years of age.

The reduction of LP 100 and raise of AP100 in visual electrophysiology were found in EEs in the asymmetric refractive accommodative esotropia correction group. The latency of P100 wave decrease indicates on conduction recover and the subclinical feature of the optic nerve refunction [20, 21]. The P100 wave amplitude increase confirms the retinal ganglion cells axons refunction and/ or restructure [20, 21].

Asymmetric refractive accommodative esotropia correction treatment decreased plus power of the spectacles in EEs, increased plus power of the spectacles in the DEs to maintain the ability to adjust the lens in patients. For a more rapid reduction in the degree of esotropia and maximal relaxation of the lens, the decreased plus power of spectacles can be prescribed for EEs to reduce the degree of Low- and higher-order aberration[9]. At the initiation of the asymmetric refractive accommodative esotropia correction treatment, the increased plus power of the spectacles was relatively higher which may have inhibited the effects of visual acuity in the DEs. Blurred DEs by increased plus power of the spectacles work like patching effects. With the treatment of both EEs and DEs, the visual acuity of both eyes improved gradually to increase deviation to 83 PD at near vision and 86 at distance vision with glasses at the end of this study. The anisometropia decreased to 0.14 D of the spherical equivalent at the 24-month by treated both EEs and DEs simultaneously. There was no data on the cycloplegic refraction during the study because cycloplegia cause a transient hyperopia which might be influenced by gradual relaxation of the ciliary muscle tone or completely damp ciliary muscular fibers activity[22], frequently cycloplegia make the lens being shorter which damage the hyperopic eye[8].

Our results confirmed that gains in the visual acuity and reductions in both deviation and anisometropia were attributable to the asymmetric refractive accommodative esotropia correction as an effective treatment for residual refractive accommodative esotropia. The resolution of anisometropia is mediated by decreasing plus power of the spectacles in EEs and increasing plus power of the spectacles in DEs to maintain ocular accommodation and decrease anisometropia. Asymmetric refractive accommodative esotropia correction treatment reduces the degree of anisometropia more rapidly and maximally relaxes the lens and reduces anti-accommodation in refractive accommodative esotropia[8]. Treatment outcome was not related to age, sex, or prior treatment history, but were related to better baseline binocular vision and visual acuity.

CONCLUSIONS

In conclusion, our results demonstrate that the asymmetric refractive accommodative esotropia correction is an effective esotropia therapy to accelerate improvement in children with residual refractive accommodative esotropia.

ACKNOWLEDGMENTS

This study was supported by Asia Pediatric Ophthalmologist Association.

References

1. Lambert, S.R., *Accommodative esotropia*. Ophthalmol Clin North Am, 2001. 14(3): p. 425-32.
2. Lowery, R.S., A. Hutchinson, and S.R. Lambert, *Emmetropization in accommodative esotropia: an update and review*. Compr Ophthalmol Update, 2006. 7(3): p. 145-9.
3. Swan, K.C., *Accommodative esotropia long range follow-up*. Ophthalmology, 1983. 90(10): p. 1141-5.
4. Swan, K.C., *Accommodative esotropia: summary and conclusions*. Trans Am Acad Ophthalmol Otolaryngol, 1957. 61(3): p. 395-6.
5. Swan, K.C., *Accommodative esotropia: classification and diagnosis*. Trans Am Acad Ophthalmol Otolaryngol, 1957. 61(3): p. 383-9.
6. Mulvihill, A., et al., *Outcome in refractive accommodative esotropia*. Br J Ophthalmol, 2000. 84(7): p. 746-9.
7. Zhisheng Li, G.L., Zueqiang Li, Na Xue, Lavonne Rayer Lee, Daina Danlai Fung, *Treatment of anisometropic amblyopia in children with automatic frequenc conversion laser*. J Clin Exp Ophthalmol, 2019. 10(2): p. 1-8.
8. Zhisheng Li, Z.Z., Geng Li, Zueqiang Li, Na Zue, Liangjun Sun, Huifang Zheng, Bensheng Qiu, Jiahong Gao, Diana Danlai Fung, *A randomized clinical trail of asymmetric anisometropic correction for anisometropic amblyopia in children aged 4 to 12 years*. Ophthamology Research, 2020. 2(1): p. 1-11.
9. Zhisheng, L., *Children Ocular Refraction and Amblypia*. 2013, Hong Kong: Hong Kong New Youth Press.
10. Preslan, M.W. and G.R. Beauchamp, *Accommodative esotropia: review of current practices and controversies*. Ophthalmic Surg, 1987. 18(1): p. 68-72.
11. Esposito Veneruso, P., D. Bruzzese, and A. Magli, *Long-term development of refractive error in refractive, nonrefractive and partially accommodative esotropia*. PLoS One, 2018. 13(9): p. e0204396.
12. Lambert, S.R. and M.J. Lynn, *Longitudinal changes in the spherical equivalent refractive error of children with accommodative esotropia*. Br J Ophthalmol, 2006. 90(3): p. 357-61.
13. Troilo, D., *Neonatal eye growth and emmetropisation--a literature review*. Eye (Lond), 1992. 6 (Pt 2): p. 154-60.
14. Ingram, R.M., L.E. Gill, and T.W. Lambert, *Effect of spectacles on changes of spherical hypermetropia in infants who did, and did not, have strabismus*. Br J Ophthalmol, 2000. 84(3): p. 324-6.
15. Baker, J.D. and M.M. Parks, *Early-onset accommodative esotropia*. Am J Ophthalmol, 1980. 90(1): p. 11-8.
16. Mutti, D.O., *To emmetropize or not to emmetropize? The question for hyperopic development*. Optom Vis Sci, 2007. 84(2): p. 97-102.
17. Cotter, S.A., *Management of childhood hyperopia: a pediatric optometrist's perspective*. Optom Vis Sci, 2007. 84(2): p. 103-9.
18. Yang, H.K., et al., *Changes in refractive errors related to spectacle correction of hyperopia*. PLoS One, 2014. 9(11): p. e110663.
19. Donahue, S.P., *Prescribing spectacles in children: a pediatric ophthalmologist's approach*. Optom Vis Sci, 2007. 84(2): p. 110-4.
20. Holder, G.H., *Localizing lesions in the visual system*. In: Heckenlively JR, Arden GB eds *Principles and practice of clinical electrophysiology of vision*. . 2006: p. 12.
21. Lachowicz, E., et al., *The electrophysiological tests in the early detection of the visual pathway dysfunction in patients with microadenoma*. Doc Ophthalmol, 2021.
22. Black, B.C., *The influence of refractive error management on the natural history and treatment outcome of accommodative esotropia (an American Ophthalmological Society thesis)*. Trans Am Ophthalmol Soc, 2006. 104: p. 303-21.

**Table 1. Baseline Demographic and Clinical Characteristics at Enrollment
(N=72)**

	Treated (N=36)		Control (N=36)	
	Frequency	Percent	Frequency	Percent
Gender				
Female	17	47.2	17	47.2
Age				
4 to <5 years	4	11.1	0	0.0
5 to <6 years	15	41.7	2	5.6
6 to <7 years	8	22.2	2	5.6
7 to <8 years	5	13.9	5	13.9
8 to <9 years	2	5.6	8	22.2
9 to <10 years	1	2.8	7	19.4
10 to <11 years	1	2.8	5	13.9
Mean (SD) year	5.64(1.94)		5.81(1.39)	
Number with Anisometropia				
No. of patients	12	33.3	11	30.6
Refractive Accommodative Esotropia Eye				
Right eye	16	44.4	15	41.7
Left eye	20	55.6	21	58.3
Prior Treatment Spectacles				
1 year	18	50.0	15	41.7
2 years	9	25.0	12	33.3
3 years	6	16.7	7	19.4
4 years	3	8.3	2	5.6
Mean (SD) year	1.83(1.00)		1.89(1.00)	
Patching				
0 year	1	2.8	2	5.6
1 year	17	47.2	13	36.1
2 years	8	22.2	12	33.3
3 years	7	19.4	7	19.4
4 years	3	8.3	2	5.6
Mean (SD) year	1.83(1.06)		1.84(1.01)	
Atropine				
0 year	26	72.2	22	61.1
1 year	10	27.8	13	36.1
2 years	0	0.0	1	2.8
Mean (SD) year	0.28(0.45)		0.42(0.55)	
Visual Training				
0 year	4	11.1	3	8.3
1 year	15	41.7	15	41.7
2 years	10	27.8	12	33.3
3 years	6	16.7	4	11.1
4 years	1	2.8	2	5.6
Mean (SD)	1.58(1.00)		1.64(0.99)	
Deviation (pd without glasses)				
Distance				
10	3	8.3	2	5.6
15	16	44.4	17	47.2

20	11	30.6	12	33.3
25	3	8.3	3	8.3
30	2	5.6	1	2.8
35	1	2.8	1	2.8
Mean (SD) PD	18.33(5.61)		18.19(5.09)	
Near				
15	4	11.1	8	22.2
20	17	47.2	13	36.1
25	10	27.8	10	27.8
30	2	5.6	3	8.3
35	3	8.3	2	5.6
Mean (SD) PD	22.64(5.28)		21.94(5.51)	
Deviation (pd with glasses)				
Distance				
10	3	8.3	2	5.6
15	17	47.2	17	47.2
20	9	25.0	12	33.3
25	4	11.1	3	8.3
30	2	5.6	1	2.8
35	1	2.8	1	2.8
Mean (SD) PD	18.33(5.73)		18.19(5.09)	
Near				
15	5	13.9	7	19.4
20	16	44.4	15	41.7
25	9	25.0	9	25.0
30	3	8.3	3	8.3
35	3	8.3	2	5.6
Mean (SD) PD	22.64(5.54)		21.94(5.38)	

Table 2 . Deviation and No. of Treatment Days of Refractive Accommodative Esotropia Eye in Treatment Group (N=36)

	40-day exam		3-month exam		6-month exam		12-month exam		24-month exam	
	Frequ	Perc	Frequ	Perc	Frequ	Perc	Frequ	Perc	Frequ	Perc
	ency	ent	ency	ent	ency	ent	ency	ent	ency	ent
Distribution of Deviation n(%)										
(pd without glasses)										
Distance										
0	0	0.0	0	0.0	0	0.0	10	27.8	24	66.7
5	0	0.0	1	2.8	13	36.1	15	41.7	9	25.0
10	5	13.9	15	41.7	13	36.1	8	22.2	2	5.6
15	20	55.6	12	33.3	7	19.4	3	8.3	1	2.8
20	6	16.7	5	13.9	3	8.3	0	0.0	0	0.0
25	2	5.6	3	8.3	0	0.0	0	0.0	0	0.0
30	3	8.3	0	0.0	0	0.0	0	0.0	0	0.0
Mean (SD) PD	16.94(5.38)		14.17(5.00)		10.00(4.78)		5.56(4.60)		2.22(3.67)	
Near										
0	0	0.0	0	0.0	0	0.0	4	11.1	17	47.2
5	0	0.0	0	0.0	1	2.8	7	19.4	7	19.4
10	0	0.0	1	2.8	13	36.1	14	38.9	9	25.0
15	5	13.9	15	41.7	13	36.1	8	22.2	2	5.6
20	19	52.8	12	33.3	6	16.7	3	8.3	1	2.8
25	7	19.4	5	13.9	3	8.3	0	0.0	0	0.0
30	2	5.6	3	8.3	0	0.0	0	0.0	0	0.0
35	3	8.3	0	0.0	0	0.0	0	0.0	0	0.0
Mean (SD) PD	22.08(5.40)		19.17(5.00)		14.58(4.98)		9.86(5.54)		4.86(5.54)	
(pd with glasses)										
Distance										
0	0	0	0	0	1	2.8	31	86.1	31	86.1
5	0	0.0	10	27.8	16	44.4	5	13.9	5	13.9
10	8	22.2	17	47.2	15	41.7	0	0.0	0	0.0
15	17	47.2	4	11.1	3	8.3	0	0.0	0	0.0
20	6	16.7	5	13.9	1	2.8	0	0.0	0	0.0
25	3	8.3	0	0.0	0	0.0	0	0.0	0	0.0
30	2	5.6	0	0.0	0	0.0	0	0.0	0	0.0
Mean (SD) PD	16.39(5.43)		10.56(4.90)		8.19(3.99)		4.86(3.87)		0.69(1.75)	
Near										
0	0.9									
0	0	0	0	0	1	2.8	11	30.6	30	83.3
5	0	0.0			3	8.3	7	19.4	3	8.3
10	0	0.0	11	30.6	21	58.3	13	36.1	3	8.3
15	8	22.2	16	44.4	8	22.2	5	13.9	0	0.0
20	16	44.4	5	13.9	3	8.3	0	0.0	0	0.0
25	7	19.4	4	11.1	0	0.0	0	0.0	0	0.0
30	3	8.3	0	0.0	0	0.0	0	0.0	0	0.0
35	2	5.6	0	0.0	0	0.0	0	0.0	0	0.0
Mean (SD) PD	21.53(5.45)		15.28(4.77)		11.25(4.20)		6.67(5.35)		1.25(3.02)	
No. of Treatment Days/Month, n(%)										
0	0	0.0	2	5.6	2	5.6	0	0.0	0	0.0
5	7	19.4	0	0.0	0	0.0	0	0.0	0	0.0

10	15	41.7	15	41.7	20	55.6	30	83.3	34	94.4
15	10	27.8	0	0.0	0	0.0	0	0.0	0	0.0
20	4	11.1	9	25.0	13	36.1	6	16.7	2	5.6
30	0	0.0	3	8.3	1	2.8	0	0.0	0	0.0
40	0	0.0	7	19.4	0	0.0	0	0.0	0	0.0
Mean (SD)										
Treatment Days	11.52(4.60)		19.44(12.41)		13.61(6.39)		11.67(3.78)		10.56(2.32)	

Table 3. Comparison of Visual Acuity, Interocular Acuity Difference, Refractive Error, Anisometropia and Improvement Line Between Treatment Group and Control Group (n=72)

Mean (SD)	1 Day		40 Day		3 Month		6 Month		12 Month		24 Month	
	Treated	Control	Treated	Control	Treated	Control	Treated	Control	Treated	Control	Treated	Control
Best-corrected visual acuity (Letter)												
EE*	72.0 8(16.62)	71.2 5(13.54)	91.2 5(9.21)	71.2 5(13.54)	98.0 6(6.24)	72.3 6(13.65)	102. 50(4.71)	73.7 5(14.21)	106. 39(3.71)	74.7 2(15.07)	108. 06(2.47)	78.8 9(16.39)
DE**	88.1 9(7.84)	88.0 6(7.86)	100. 14(6.38)	88.0 6(7.86)	105. 00(5.35)	89.0 3(8.60)	107. 36(3.48)	90.8 3(8.41)	108. 75(2.50)	92.9 2(7.87)	109. 31(1.75)	96.6 7(7.38)
Best-corrected interocular acuity difference lines												
EE	3.22(3.39)	3.36(2.51)	1.81(1.94)	3.36(2.51)	1.39(1.36)	3.33(2.56)	0.97(1.03)	3.42(2.76)	0.47(0.74)	3.64(2.92)	0.25(0.44)	3.56(3.03)
DE	5.03(2.75)	6.72(1.34)	4.69(1.95)	6.60(1.30)	4.22(1.83)	6.56(1.34)	3.71(1.69)	6.31(1.33)	3.05(1.57)	5.86(1.41)	2.49(1.39)	5.31(1.40)
Anisometropia (Calculated Difference in spheric	6.76(2.32)	5.08(1.85)	3.80(2.11)	4.97(1.85)	3.57(1.89)	4.93(1.88)	3.32(1.73)	4.64(1.88)	2.77(1.41)	4.08(1.87)	2.35(1.29)	3.32(1.87)
	1.65(1.78)	1.64(1.55)	0.89(1.23)	1.63(1.57)	0.65(1.00)	1.63(1.56)	0.39(0.79)	1.67(1.56)	0.28(0.74)	1.78(1.64)	0.14(0.41)	1.92(1.73)

al
equival
ent) (D)

Improv
ement
lines
from
baselin
e to
best
measur
ed
acuity

EE	0.00	0.00	4.00(2.27)	0.00	5.36(2.71)	0.22(0.42)	6.25(2.82)	0.39(0.55)	7.03(2.99)	0.58(0.69)	7.36(3.24)	1.42(0.94)
DE	0.00	0.00	2.33(1.07)	0.00	3.36(0.90)	0.22(0.42)	3.86(1.25)	0.44(0.50)	4.25(1.44)	0.86(0.49)	4.36(1.61)	1.58(0.60)

*: Refractive Accommodative Esotropia Eye; **: Dominated Eye



