

Original research

The effect of different amblyopia treatment protocols on axial length of non-amblyopic eyes in anisohyperopic patients

Monireh Ghasempour^a, Masoud Khorrami-Nejad^{a,b,*}, Mohamad Reza Akbari^b,
Mohamad Aghazadeh Amiri^a

^a Department of Optometry, School of Rehabilitation, Shahid Beheshti University of Medical Science, Tehran, Iran

^b Eye Research Center, Farabi Eye Hospital, Tehran University of Medical Science, Tehran, Iran

Received 10 April 2018; revised 22 August 2018; accepted 5 September 2018

Available online 29 September 2018

Abstract

Purpose: To evaluate the effect of full-time and part-time occlusion therapy on axial length (AL) of non-amblyopic eyes in anisohyperopic patients.

Methods: Sixty-five patients who were treated for anisohyperopic amblyopia were recruited for this prospective cross-sectional study. Treatment was provided as patching of the non-amblyopic for 4 h or less (part-time occlusion therapy, n = 42), patching of the non-amblyopic for 8 h or more (full-time occlusion therapy, n = 13) and refractive correction (spectacles, non-patched group, n = 10). AL measurements were calculated by a Lenstar LS 900 at the last session of amblyopia therapy.

Results: The mean age of patients treated for anisohyperopic amblyopia was 4.90 ± 0.80 years, and the mean follow-up period was 1.50 ± 0.80 years. The mean of spherical equivalent in amblyopic and non-amblyopic eyes were $+3.58 \pm 2.26$ and $+1.84 \pm 0.97$ diopter (D) before treatment, and $+3.21 \pm 2.28$ and $+1.49 \pm 0.99$ D after treatment, respectively. The mean of spherical equivalent in non-amblyopic eyes before (F = 0.452, df = 2, P = 0.639) and after (F = 0.190, df = 2, P = 0.828) treatment did not have any significant difference between the three groups. The mean AL of amblyopic and non-amblyopic eyes were 22.11 ± 93.0 and 22.68 ± 1.07 mm, respectively. The mean AL of the non-amblyopic eye was significantly higher in the full-time occlusion therapy group when compared to the part-time patch and the non-patched groups (P < 0.001). The mean AL of amblyopic eyes showed no difference across the three treatment groups (P = 0.840).

Conclusions: The results show that a longer AL in the non-amblyopic eye, but not the amblyopic eye, can be expected with longer daily hours of patching in anisohyperopic patients. Future studies are needed to evaluate the effect of patching on AL in children with anisohyperopic amblyopia.

Copyright © 2018, Iranian Society of Ophthalmology. Production and hosting by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Keywords: Anisometropic amblyopia; Eye axial length; Occlusion therapy

Introduction

Amblyopia is a visual impairment that is characterized by a unilateral or bilateral reduction of visual acuity without an organic cause.^{1–3} With a prevalence of up to 3.5%, amblyopia is the most common cause of childhood vision loss^{4–8} that occurs in up to two-thirds of anisometropic and strabismic patients.^{9–11} Anisometropia is defined as the difference of refractive power between the two eyes, frequently caused by a difference in axial length (AL).¹²

Disclosure: There is no financial interest for the authors in any methods or materials mentioned in this article.

* Corresponding author. School of Rehabilitation, Damavand St., Tehran, 1616913111, Iran.

E-mail address: op_khorrami@yahoo.com (M. Khorrami-Nejad).

Peer review under responsibility of the Iranian Society of Ophthalmology.

<https://doi.org/10.1016/j.joco.2018.09.003>

2452-2325/Copyright © 2018, Iranian Society of Ophthalmology. Production and hosting by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Early diagnosis and timely treatment of anisometropic amblyopia are crucial in the successful treatment of this condition.^{13–16} Treatment of amblyopic anisometropia usually involves correcting the refractive errors and covering the non-amblyopic eye using a patch, i.e., occlusion therapy.^{1,6,11,16,17} Although there is no consensus about the daily length of occlusion time that can result in the best treatment outcomes, some studies have shown that the daily duration of patching is an important factor in successful treatment of amblyopia in children.^{11,18} While some studies suggest full-time occlusion therapy, others have documented improved success with part-time occlusion.^{1,11,19,20}

Hypermetropic anisometropia is a major risk factor of amblyopia.^{5,8,9,21} The AL of the more hypermetropic eye is shorter than emmetropic or less hypermetropic eye.²² There are reports in the literature indicating that experimental intervention can lead to changes in ocular AL. Experimentally-induced visual deprivation can change the AL which is demonstrated in a study by suturing rabbit eyelids together.²³ In another study, the role of early surgical treatment of congenital ptosis is highlighted for prevention of axial elongation.²⁴

According to findings of previous studies, it can be suggesting that children with anisohyperopic amblyopia, patching of the non-amblyopic eye during the critical or sensitive period, may affect the AL of the dominant (non-amblyopic) eye. Therefore, this study sets out to investigate the effect of full-time and part-time occlusion therapy on the AL of non-amblyopic in anisohyperopic amblyopia.

Methods

This prospective cross-sectional study (descriptive-analytical) was performed at the School of Rehabilitation, Shahid Beheshti University of Medical Sciences and Najafzadeh Eye Clinic between April 2016 and July 2017. Sixty-five patients with anisohypermetropic amblyopia with no congenital anomalies, organic amblyopia, strabismus, and visual deprivation amblyopia who received their first treatment for amblyopia at the mean age of 4.90 ± 0.80 years old were selected as the sample size. The study was performed in accordance with the tenets of the Declaration of Helsinki and was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences.

Amblyopia was defined as having one eye with the best corrected distance visual acuity (BCDVA) of 20/30 or worse resulting from hyperopic anisometropia and a difference of two or more lines in visual acuity between the two eyes. Bilateral ocular AL measurements were performed for all patients using a Lenstar LS 900 (HaagStreit AG Switzerland) at the last session of amblyopia therapy. Visual acuity was recorded in logMAR system. Strabismus was assessed using cover–uncover test and alternate cover tests. Refractive errors were measured on a Nidek ARK-710A auto kerato-refractometer (Nidek Co. Ltd, Gamagori, Japan) and a HEINE BETA 200 retinoscope (HEINE Optotechnic, Hersching, Germany). All participants underwent

cyclorefraction by administering cyclopentolate 1% (two drops, 5 min apart followed by refraction 30 min after the last drop).

Hypermetropia was defined as a cycloplegic refractive error greater than or equal to 1.00 diopter (D), and anisometropia was defined when hyperopic refractive error difference between the eyes was more than or equal to 1.00 D in cycloplegic refraction.

The treatment protocol has been reported previously.^{6,11,16,17} During the first stage of treatment, all amblyopic subjects were dispensed with refractive correction in the form of spectacles. Occlusion therapy was not attempted at this stage. The first follow-up session was held one month after the initial eye examination. Children were re-assessed for amblyopia and prescribed with new pair of glasses when needed prior to commencing amblyopia therapy in the form of occlusion therapy. Follow-up visits were continued until amblyopia was completely resolved.

Treatment was provided as occlusion therapy of the non-amblyopic eyes for 4 h or less (part-time occlusion therapy, $n = 42$), occlusion therapy of the non-amblyopic eyes for 8 h or more (full-time occlusion therapy, $n = 13$), and refractive correction (spectacles, no occlusion therapy, $n = 10$). Occlusion therapy was accompanied by an hour of engagement in near vision tasks. Mean equivalent spherical refraction and BCDVA in logMAR system were recorded.

Statistical analysis was performed using SPSS version 22.0 software for Windows (IBM Inc, Armonk, New York, NY, USA). Data were tested for normality of distribution using the Shapiro-Wilk test. The one-way analysis of variance (ANOVA) test was used to examine the relationship between the three treatment groups ($P > 0.05$ for homogeneity of variance among groups, and post-hoc multiple comparisons when $P < 0.05$). The sensitivity of the tests was set at 95% (significance reached if $P < 0.05$).

Results

The mean age of 65 anisohyperopic amblyopia patients was 4.90 ± 0.80 years, and 40 (61.5%) of these patients were male. The mean length of treatment for amblyopia for all participants was 1.50 ± 0.80 years. Occlusion therapy in part-time and full-time occlusion therapy were continued for an average of 1.80 ± 0.23 years and 2.10 ± 1.50 years, respectively. All patients in non-patched group wore refractive correction four months before measuring AL.

The mean of BCDVA (in logMAR system) for amblyopic and non-amblyopic eyes were 0.40 ± 0.17 and 0.01 ± 0.01 before treatment, and 0.08 ± 0.07 and 0.05 ± 0.03 after treatment, respectively. The mean of BCDVA in the non-amblyopic eyes before and after treatment in part-time and full-time occlusion therapy groups did not have any significant difference ($P = 0.766$ and $P = 0.053$, respectively).

Mean spherical equivalent in amblyopic and non-amblyopic eyes were $+3.58 \pm 2.26$ and $+1.84 \pm 0.97$ D before treatment, and $+3.21 \pm 2.28$ and $+1.49 \pm 0.99$ D after treatment, respectively. The result of one-way ANOVA test

showed that the mean of spherical equivalent in non-amblyopic eyes before treatment did not have any significant difference between the three groups ($F = 0.452$, $df = 2$, $P = 0.639$). Also, the mean spherical equivalent in non-amblyopic eyes after treatment did not have any significant difference between the three groups ($F = 0.190$, $df = 2$, $P = 0.828$). Details for spherical equivalent values (mean \pm SD) for both eyes as differentiated by patching protocol groups (treatment) are presented in Table 1.

The mean AL in amblyopic eyes was 22.11 ± 0.93 mm (range, 20.15–24.44 mm) and 22.68 ± 1.07 mm (range, 20.36–25.72 mm) in non-amblyopic eyes. The mean AL values in both eyes of different patching protocol groups are presented in Table 2.

The one-way ANOVA test showed a significant difference in the mean AL between the three groups of non-amblyopic eyes ($F = 11.833$, $df = 2$, $P < 0.001$). The results of the Scheffe post-hoc test showed that the mean AL of non-amblyopic eyes in the full-time patch therapy group was more than the two other groups ($P < 0.001$) while there was no significant difference between the part-time and no patch therapy groups ($P = 0.431$). The results of the ANOVA test showed that there was no significant difference in the mean AL between the three groups of amblyopic eyes ($F = 0.157$, $df = 2$, $P = 0.840$). Fig. 1 shows the box plot diagram for distribution of AL of amblyopic and non-amblyopic eyes, in 3 different groups of amblyopia treatment.

Discussion

Amblyopia is inherently a binocular disorder caused by an imbalance between the two eyes and resulting in the abnormal development of the visual pathways that affect both the amblyopic and the non-amblyopic fellow eye.²⁵ Anisohyperopic amblyopia is an important risk factor for amblyopia.^{5–9}

The standard treatment for anisometropic amblyopia consists of correction of refractive errors and occlusion therapy.^{1,6,11,17} The effect of duration of occlusion therapy on the efficacy of amblyopia therapy has been discussed in the literature. Both full-time and part-time occlusion therapy have advocates.^{1,11,19,20}

After the prescription of refractive correction, occlusion therapy has been accepted as the second stage of the standard treatment for anisometropic amblyopia.^{16–26} The general efficacy of part-time and full-time occlusion therapy according to the severity of amblyopia for best treatment outcomes has been established.^{11,25,27,28}

Current literature, to the best of authors' knowledge, does not provide any evidence about changes in AL following occlusion therapy. The results indicate that in individuals with anisohyperopic amblyopia, full-time occlusion therapy may induce elongation of AL in the occluded (non-amblyopic) eye, thereby leading to an increased discrepancy between the AL of the two eyes (aniso-AL). Our results also demonstrate a significant difference in the mean AL of non-amblyopic eyes between the three groups of amblyopia treatment. The mean AL in the full-time occlusion therapy group was greater than the part-time occlusion therapy and the non-patched group. Meanwhile, there was no difference in AL between the treatment groups for the AL of the amblyopic eyes. Hence, with an increase in the AL of the dominant non-amblyopic eye, and in the absence of AL change in the more hypermetropic eye (the amblyopic eye), an increase in the difference in AL between the two eyes may occur, leading to modified interocular interactions.²⁹

Interestingly, our findings in full-time occlusion therapy group suggest that despite the mean AL of the non-amblyopic eye after the treatment of amblyopia was longer than the amblyopic eye, no significant change was seen in the refractive error of the eye closed during occlusion therapy. This finding

Table 1
Mean, standard deviation (SD), and range of spherical equivalent in different patching protocol after the treatment of amblyopia.

Patching protocol		Number	Minimum	Maximum	Mean \pm SD	P-value
No patching	Non-amblyopic eye	10	+0.87	+3.75	+1.66 \pm 0.95	0.155
	Amblyopic eye	10	+0.50	+3.75	+1.94 \pm 1.04	
Partial time patching	Non-amblyopic eye	42	0.00	+3.62	+1.48 \pm 0.88	>0.001
	Amblyopic eye	42	-0.37	+5.00	+2.50 \pm 1.38	
Full time patching	Non-amblyopic eye	13	-0.50	+3.75	+1.40 \pm 1.39	>0.001
	Amblyopic eye	13	+1.87	+10.62	+6.47 \pm 2.41	

SD: Standard deviation.

Table 2
Mean, standard deviation (SD), and range of axial length (AL) in different patching protocol after the treatment of amblyopia.

Patching protocol		Number	Minimum	Maximum	Mean \pm SD	P-value
No patching	Non-amblyopic eye	10	20.68	22.93	22.07 \pm 0.72	$P = 0.876$
	Amblyopic eye	10	20.72	22.92	22.06 \pm 0.70	
Partial time patching	Non-amblyopic eye	42	20.36	24.22	22.50 \pm 0.76	$P < 0.001$
	Amblyopic eye	42	20.15	24.43	22.16 \pm 0.82	
Full time patching	Non-amblyopic eye	13	21.58	25.72	23.77 \pm 1.45	$P < 0.001$
	Amblyopic eye	13	20.17	24.44	21.99 \pm 1.42	

SD: Standard deviation.

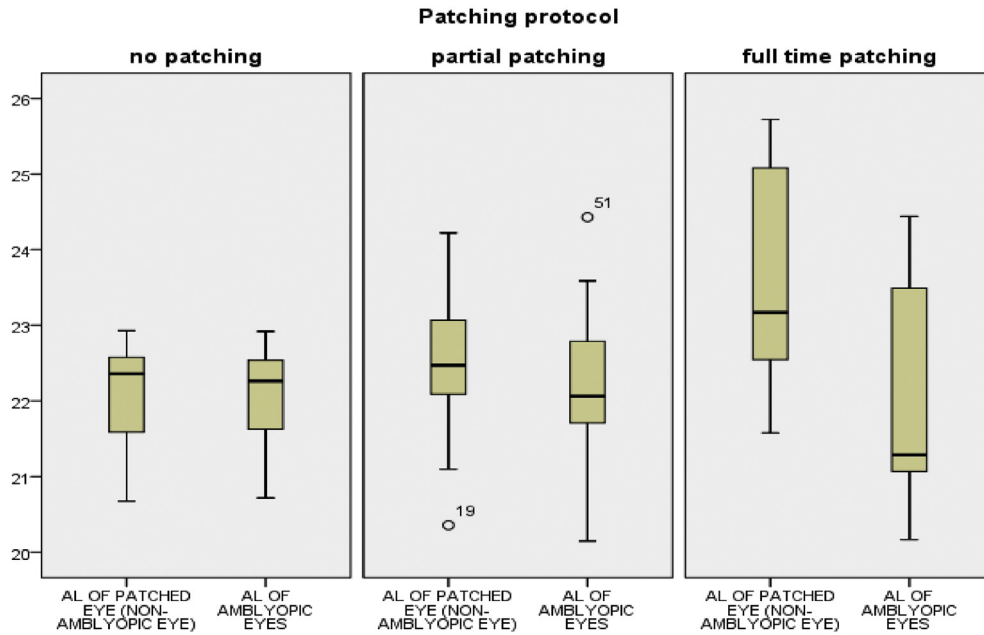


Fig. 1. Box plot diagram of distribution of axial length (AL) of both eyes in 3 different groups.

can be explained by the effect of different factors on the refractive status of human eye including AL, corneal refractive power, and position of the crystalline lens.²⁴ It may be possible that the change in refractive power of the eye which is caused by the increase in AL, have been compensated by factors not investigated in this study.³⁰ The unknown interaction of different factors on the final refractive power of eye can be evaluated in future studies.

Results of this study and previous studies suggest that visual deprivation may lead to an increase in AL of the non-amblyopic eye during amblyopia therapy. Moreover, the longer time of patching results in a greater probability of AL increase. These findings may provide additional insight into the underlying causes of poorer outcomes reported following full-time occlusion therapy.¹⁹ It has been established that visual deprivation can increase ocular AL. In a study by Hoyt et al., ptosis caused by third nerve palsy or eyelid hemangiomas resulted in axial elongation in infants.²⁴ Verolino et al. demonstrated on a rabbit model that the AL increased when eyelids were sutured together.²³

One of the main limitations of this study was measuring AL only after treatment of amblyopia, and the other one was a small sample size of the treatment group without occlusion therapy. This study was a pilot study with strong limitations that suggested further studies in this subject.

It can be suggested that other methods such as pharmacological and optical penalization or the active methods of vision therapies be tried rather than full-time occlusion therapy. These new trends may prevent the non-amblyopic eye from visual deprivation resulting from excessive occlusion therapy. The results of this study can be further verified through measurement of AL before and after occlusion therapy.

References

1. Cotter SA. Treatment of anisometric amblyopia in children with refractive correction. *Ophthalmology*. 2006;113(6):895–903.
2. Avram E, Stănilă A. Functional amblyopia. *Oftalmologia*. 2013;57(4):3–8.
3. Žiak P, Holm A, Halička J, Mojžiš P, Piñero DP. Amblyopia treatment of adults with dichoptic training using the virtual reality Oculus Rift head mounted display: preliminary results. *BMC Ophthalmol*. 2017;17(1):105.
4. Stewart CE, Fielder AR, Stephens DA, Moseley MJ. Treatment of unilateral amblyopia: factors influencing visual outcome. *Invest Ophthalmol Vis Sci*. 2005;46(9):3152–3160.
5. Ehrlich MI, Reinecke RD, Simons K. Preschool vision screening for amblyopia and strabismus programs, 1983 programs, methods, guidelines. *Surv Ophthalmol*. 1983;28(3):145–163.
6. Kaphle D, Shrestha JB, Paudel P. Treatment of anisometric amblyopia in children with refractive correction. *J Inst Med*. 2010;31(2):214–218.
7. Roberts CJ, Adams GG. Contact lenses in the management of high anisometric amblyopia. *Eye*. 2002;16(5):577.
8. Warkad VU, Panda L, Behera P, Das T, Mohanta BC, Khanna R. The Tribal Odisha Eye Disease Study (TOES) I: prevalence and causes of visual impairment among tribal children in an urban school in Eastern India. *J Am Assoc Pediatr Ophthalmol Strabismus*. 2018;22(2), 145.e1-e145.e6.
9. Toor SS, Horwood AM, Riddell PM. Anisometric amblyopia: factors influencing the success or failure of its treatment. *Br Ir Orthopt J*. 2015;9:9–16.
10. Barrett BT, Bradley A, Candy TR. The relationship between anisometropia and amblyopia. *Prog Retin Eye Res*. 2013;36:120–158.
11. Khorrami-Nejad M, Akbari MR, Khosravi B. The prevalence of strabismus types in strabismic Iranian patients. *Clin Optom*. 2018;10:19–24.
12. Patel VS, Simon JW, Schultze RL. Anisometric amblyopia: axial length versus corneal curvature in children with severe refractive imbalance. *J Am Assoc Pediatr Ophthalmol Strabismus*. 2010;14(5):396–398.
13. Wu C, Hunter DG. Amblyopia: diagnostic and therapeutic options. *Am J Ophthalmol*. 2006;141(1):175–184.
14. Hunter D, Cotter S. Early diagnosis of amblyopia. *Vis Neurosci*. 2018;35: E013.

15. Feng L, Candy TR, Yang Y. Severe myopic anisometropia in a Chinese family. *Optom Vis Sci.* 2012;89(4):507–511.
16. Stewart CE, Stephens DA, Fielder AR, Moseley MJ. Objectively monitored patching regimens for treatment of amblyopia: randomised trial. *Br Med J.* 2007;335(7622):707.
17. Simons K. Amblyopia characterization, treatment, and prophylaxis. *Surv Ophthalmol.* 2005;50(2):123–166.
18. Wang J. Compliance and patching and atropine amblyopia treatments. *Vis Res.* 2015;114:31–40.
19. Woodruff G, Hiscox F, Thompson JR, Smith LK. Factors affecting the outcome of children treated for amblyopia. *Eye.* 1994;8(6):627.
20. Stanković B. Clinical aspects of different types of amblyopia. *Vojnosanit Pregl.* 2011;68(8):696–698.
21. Smith III EL, Hung LF, Arumugam B, Wensveen JM, Chino YM, Harwerth RS. Observations on the relationship between anisometropia, amblyopia and strabismus. *Vis Res.* 2017;134:26–42.
22. Hoshikawa R, Ito M, Yano T, Tsutsui K, Sato T, Shimizu K. Association between ocular dominance and anisometropic hyperopia. *Am Orthopt J.* 2016;66(1):107–113.
23. Verolino M, Nasti G, Sellitti L, Costagliola C. Axial length increase in lid-sutured rabbits. *Surv Ophthalmol.* 1999;44:S103–S108.
24. Hoyt CS, Stone RD, Fromer C, Billson FA. Monocular axial myopia associated with neonatal eyelid closure in human infants. *Am J Ophthalmol.* 1981;91(2):197–200.
25. Jia W, Lan F, Zhao X, et al. The effects of monocular training on binocular functions in anisometropic amblyopia. *Vis Res.* 2017 Jun 27. <https://doi.org/10.1016/j.visres.2017.02.008> (Epub ahead of print).
26. Repka MX, Holmes JM. Lessons from the amblyopia treatment studies. *Ophthalmology.* 2012;119(4):657–658.
27. Vagge A, Nelson LB. Compliance with the prescribed occlusion treatment for amblyopia. *Curr Opin Ophthalmol.* 2017;28(5):454–459.
28. Pediatric Eye Disease Investigator Group. A comparison of atropine and patching treatments for moderate amblyopia by patient age, cause of amblyopia, depth of amblyopia, and other factors. *Ophthalmology.* 2003;110(8):1632–1637.
29. Lai XJ, Alexander J, He M, Yang Z, Suttle C. Visual functions and interocular interactions in anisometropic children with and without amblyopia. *Invest Ophthalmol Vis Sci.* 2011;52(9):6849–6859.
30. Park SH, Park KH, Kim JM, Choi CY. Relation between axial length and ocular parameters. *Ophthalmologica.* 2010;224(3):188–193.