

Is There a Critical Period for Amblyopia Therapy? Results of a Study on Older Anisometric Amblyopes

TASKIN KHAN

ABSTRACT

Purpose: Amblyopia, a common cause of low vision, is rarely treated in adults. Improvement in vision has been seen beyond the critical period at times. Hence, this study was taken up to study the effect of minimal occlusion therapy (2-4 hours/day) in anisometric amblyopic patients in the age group of 12-30 years.

Materials and Methods: The study is a prospective, randomized case series of anisometric amblyopia patients aged 12-30 years who reported in the outpatient department of Hakeem Abdul Hameed Centenary Hospital, New Delhi, from December 2011 to November 2013. Thorough ocular examination and cycloplegic refraction was done to rule out other ocular disease. Anisometric Amblyopia was diagnosed only after four weeks of spectacle wear. The selected patients were then advised occlusion therapy of 2-4 hours per day of better eye with stress on near visual task. Videogames, computers, mobile phone gaming and colouring in especially designed patterns were used

as vision training aids. The outcome measure selected was best corrected visual acuity (BCVA) achieved that remained stable for three consecutive months of occlusion.

Results: Sixty one patients of anisometric amblyopia were included in the study (32 males and 29 females) aged 12-30 years (mean age 17 years). Mean BCVA at the start of treatment was 20/125 (0.8 log MAR units) and 20/32 (0.2 log MAR units) at the end of the treatment. Thirty three patients (54%) out of 61 had BCVA of 20/20, while 58 patients (95%) had \geq 20/40 BCVA, 01(1.6%) had 20/50 and 02 (3.27%) had 20/80 BCVA at the end of therapy. The results were statistically significant (p-value $<$ 0.0001) with a 95% confidence interval.

Conclusion: This study clearly proves that there is no critical period for the treatment in older (12-30 years) anisometric amblyope. Even 2-4 hours per day of occlusion of better eye with vision training thorough near visual task of amblyopic eye is effective. However, counseling and patient compliance is important for successful outcome of therapy.

Keywords: Anisometropia, Occlusion therapy, Visual acuity

INTRODUCTION

Amblyopia or lazy eye is a unilateral or bilateral decrease in visual acuity, caused by deprivation of form sense of vision during the critical period of development resulting in abnormal binocular interaction, or both, for which no organic cause can be detected on routine ophthalmic examination [1]. Amblyopia is a common cause of monocular low vision in childhood and adults [2]. It is seen in 2-4% of the general population [1,3]. Common amblyogenic factors are strabismus, anisometropia, mixed type and visual deprivation. A defect in primary visual cortex is thought to be responsible for the development of amblyopia, though extra striate areas may also be responsible [4]. Until recently, it was thought that inadequate or abnormal stimulation of the visual system during critical early period of visual development (before 7 years) results in amblyopia [5]. Full time occlusion therapy before the critical period is considered to be the mainstay of treatment [5]. Hence, amblyopia treatment is rarely advised to older children. It was thought that the neuronal circuits stabilize during this critical period with no change occurring beyond that age. However, recently a number of studies have shown that amblyopic patients beyond the critical period can show visual improvement [6,7]. Instances have been reported where improvement in visual function is seen in an amblyopic eye if the non-amblyopic eye loses vision [8-10]. These reports point towards neuronal plasticity of adult brain with amblyopia, which helps in improvement of loss of visual function even after visual maturation. Neuronal plasticity can be demonstrated by perceptual learning, where it has been shown that repeated practicing of a difficult task can improve visual performance [11,12].

Amblyopia is a common public health problem. A large number of adult amblyopes are denied treatment because of long standing beliefs. Recent developments in understanding the neuronal plasticity of adult brain have shown that repeated practicing of near

work task can improve visual performance. The present study was done to evaluate minimal occlusion therapy of 2-4 hours in visual improvement of anisometric amblyopic patients in age group of 12-30 years.

MATERIALS AND METHODS

All patients between 12-30 years of age, reporting in ophthalmic outpatient department of Hakeem Abdul Hameed Centenary Hospital, New Delhi, between December 2011 to November 2013 that were diagnosed to have anisometric amblyopia were included in this prospective study. The patients underwent a thorough ocular examination that included recording of uncorrected visual acuity and best-corrected visual acuity (BCVA) for near and distance after cycloplegic refraction. Ocular motility, slit lamp biomicroscopy and fundus examination was done to rule out any other ocular disease. All patients underwent a trial period of one month of spectacle wear, before being diagnosed as amblyopic. Amblyopia was defined as a difference in the best-corrected visual acuity (BCVA) between the two eyes of two or more lines on the Snellen's Chart or a visual acuity of less than two lines from the normal. Anisometropia was defined as interocular difference of spherical equivalent of \geq 1D or difference of refractive astigmatism (anisoastigmatism) \geq 1.5D cylinder.

After being diagnosed as anisometric amblyopic, the patients were subjected to a counseling session before starting the treatment especially where poor compliance was suspected (older patients). Period of occlusion therapy was made flexible in older patients. A minimum of two hours (not more than four hours) of occlusion of better eye was mandatory with stress on near work task. Videogames, computers, mobile phone gaming, colouring in especially designed patterns and hand writing were used as vision training aids. A home work was assigned to younger patients who were rewarded on completion of the task. Older patients were

motivated by showing them their results on actual Snellen's scale or if not improving, the stories of other patients were shared to motivate them.

Static as well as dynamic refraction was done on each visit. Any changes in refraction were corrected to BCVA. Near visual acuity was also recorded at each visit. Follow up was done every month till normal BCVA was achieved or no change was seen for three consecutive months of occlusion. The end-point of therapy was considered as stable visual acuity maintained for a period of at least three months of occlusion. Pre and post therapy results were analysed through unpaired t-test.

RESULTS

A total of 61 patients of anisometropic amblyopia were included in the study out of which 32 were males and 29 females. Mean age was 17 years. Mean BCVA at the start of the treatment was 20/125 or 0.8 log MAR (range from 20/63 to 20/400). Out of 61 patients, 20/400 BCVA was seen in 06 patients (9.8%), 20/200 in 19(31%), 20/125 in 15(24%), 20/80 in 11(18%) and 20/63 in 10 (16%) patients before the start of therapy [Table/Fig-1]. Commonest type of anisometropia was found to be anisohyperopia 24 patients (39.3%) followed by anisoastigmatism 20 patients (32.7%) and anisomyopia 17 patients (27.8%) [Table/Fig-1-4].

Mean BCVA at the end of therapy was 20/32 or 0.2 logMAR. From the total 61 patients under study, 33(54%) had 20/20, 14(23%) had 20/25, 11(18%) had 20/40, while 01(1.6%) had 20/50 and 02 (3.27%) had 20/80 BCVA at the end of therapy [Table/Fig-1].

The patients who did not attain normal vision (20/20) included 02 patients of high anisomyopia. These were 30 year male and 28 year female with BCVA of 20/400 (1.3logMAR) and 20/200 (1 logMAR) respectively at the start of therapy and 20/80 (0.6 logMAR) at the end of the therapy. Third patient was of anisoastigmatism, a 19

year male with BCVA 20/200 (1 logMAR) at the start of therapy and 20/50 (0.4 logMAR) at the end of therapy.

Out of 61 patients, 33 (54%) had BCVA of 20/20, while 58 patients (95%) had \geq 20/40 BCVA at the end of therapy. The results were statistically significant (p-value <0.0001) with a 95% confidence interval.

Characteristics	Before Treatment	After Treatment
Total patients:	61	61
Average age of the patients	17years	17years
Number of Males	32	32
Number of Females	29	29
Mean BCVA in amblyopic eye	20/125 (0.8logMar)	20/32 (0.2 logMAR)
Range of BCVA in amblyopic eye	20/63 to 20/400	20/20 to 20/80
BCVA in amblyopic eye:	Number of patients:	
20/400	06	-
20/200	19	-
20/125	15	-
20/80	11	02
20/63	10	-
20/50	-	01
20/40	-	11
20/25	-	14
20/20	-	33
Type of Refractive Error:	Number of patients:	
Anisohyperopia	24	24
Anisoastigmatism	20	20
Anisomyopia	17	17

[Table/Fig-1]: Patient characteristics before and after treatment

S. No.	Age/Sex	Amblyopic Eye				Fellow Eye			
		BCVA Pre therapy	Log Mar Units	Prescription (SE)*	BCVA Post therapy	BCVA Pre therapy	Log Mar Units	Prescription (SE)*	BCVA Post therapy
1.	14year/F	20/80	0.6	+2DS	20/20	20/20	00	-	20/20
2.	22year/M	20/200	1.0	+4.25DS	20/40	20/25	0.1	+1.50DS	20/20
3.	30year/F	20/125	0.8	+3.50DS	20/25	20/20	00	-	20/20
4.	16year/M	20/400	02	+5.25DS	20/40	20/20	00	+1.75DS	20/20
5.	24year/M	20/200	1.0	+4DS	20/40	20/20	00	+0.5DS	20/20
6.	19year/M	20/200	1.0	+3.5DS	20/20	20/20	00	-	20/20
7.	12year/M	20/200	1.0	+4DS	20/20	20/20	00	+1.5DS	20/20
8.	30year/F	20/63	0.5	+2DS	20/20	20/20	00	-	20/20
9.	17year/M	20/63	0.5	+1.75DS	20/20	20/20	00	-	20/20
10.	14year/M	20/125	0.8	+3.25DS	20/20	20/20	00	+0.5DS	20/20
11.	12year/F	20/80	0.6	+2.75DS	20/20	20/20	00	+0.75DS	20/20
12.	17year/F	20/125	0.8	+3.50DS	20/25	20/20	00	+0.50DS	20/20
13.	12year/F	20/63	0.5	+1DS	20/20	20/20	00	-	20/20
14.	20year/M	20/63	0.5	+1.75DS	20/20	20/20	00	-	20/20
15.	20year/M	20/200	1.0	+3DS	20/25	20/20	00	-	20/20
16.	13year/F	20/400	02	+4.5DS	20/40	20/25	0.1	+1.50DS	20/20
17.	12year/F	20/80	0.6	+2.25DS	20/20	20/20	00	-	20/20
18.	12year/M	20/125	0.8	+3.50DS	20/20	20/20	00	-	20/20
19.	27year/F	20/200	1.0	+2.75DS	20/25	20/20	00	-	20/20
20.	12year/M	20/200	1.0	+4.50DS	20/20	20/25	0.1	+2.25DS	20/25
21.	20year/M	20/63	0.5	+1.75DS	20/20	20/20	00	+0.25DS	20/20
22.	20year/F	20/125	0.8	+3.25DS	20/40	20/20	00	-	20/20
23.	22year/F	20/400	02	+5.50DS	20/40	20/20	00	-	20/20
24.	13year/M	20/200	1.0	+3DS	20/20	20/20	00	-	20/20

[Table/Fig-2]: Clinical characteristics of patients with Anisohyperopia

*Spherical Equivalent

S. No.	Age/Sex	Amblyopic Eye				Fellow Eye			
		BCVA Pre therapy	Log Mar Units	Prescription	BCVA Post therapy	BCVA Pre therapy	Log Mar Units	Prescription	BCVA Post therapy
1.	23year/M	20/63	0.5	-2.25DCx90°	20/20	20/20	00	-0.75DCx90°	20/20
2.	14year/M	20/63	0.5	-1.50DCx70°	20/20	20/20	00	-	20/20
3.	28year/F	20/200	1.0	-3.25DCx180°	20/40	20/20	00	-0.5DCx160°	20/20
4.	15year/M	20/125	0.8	-3DCx180°	20/40	20/25	0.1	-1DCx180°	20/20
5.	13year/M	20/80	0.6	-2.5DCx80°	20/20	20/20	00	-1DCx90°	20/20
6.	12year/M	20/63	0.5	+2DCx90°	20/25	20/20	00	+0.50DCx90°	20/20
7.	12year/M	20/200	1.0	-3DCx80°	20/40	20/25	0.1	-1.50DCx80°	20/20
8.	12year/M	20/80	0.6	-1DS/ -2DCx90°	20/20	20/20	00	-0.50DCx60°	20/20
9.	12year/F	20/80	0.6	-3.50DCx110°	20/25	20/40	0.3	-1.50DCx180°	20/20
10.	14year/F	20/80	0.6	+2.50DCx12°	20/20	20/20	00	-0.50DS	20/20
11.	17year/F	20/125	0.8	+2DCx70°	20/20	20/20	00	-	20/20
12.	22year/F	20/200	1.0	-2.50DCx90°	20/20	20/20	00	-	20/20
13.	15year/F	20/125	0.8	-0.50DS/ -2DCx90°	20/20	20/20	00	-1.00DS	20/20
14.	18year/F	20/125	0.8	-2.75DS/ -1.75DCx90°	20/40	20/20	00	-0.75DS/ -0.25DCx90°	20/20
15.	15year/F	20/125	0.8	-3DCx120°	20/25	20/20	00	-0.75DCx60°	20/20
16.	15year/M	20/400	02	-1.00DS/ -4.25DCx180°	20/40	20/40	0.3	-1.50DCx180°	20/20
17.	18year/M	20/200	1.0	-2.25DCx90°	20/25	20/20	00	+0.50DS/ -0.50DCx90°	20/20
18.	18year/F	20/200	1.0	-0.25DS/ -2.50DCx60°	20/25	20/25	0.1	-1DCx60°	20/20
19.	19year/M**	20/200	1.0	-0.50DS/ -2.75DCx90°	20/50	20/20	00	-1.75DS	20/20
20.	15year/M	20/200	1.0	-2.75DCx80°	20/20	20/20	00	-	20/20

[Table/Fig-3]: Clinical characteristics of patients with anisoastigmatism

**Did not fulfill criteria of successful treatment

S. No.	Age/Sex	Amblyopic Eye				Fellow Eye			
		BCVA Pre therapy	Log Mar Units	Prescription (SE)*	BCVA Post therapy	BCVA Pre therapy	Log Mar Units	Prescription (SE)*	BCVA Post therapy
1.	22year/F	20/125	0.8	-4DS	20/25	20/20	00	-1DS	20/20
2.	12year/M	20/125	0.8	-3.50DS	20/20	20/20	00	-	20/20
3.	19year/F	20/63	0.5	-3.25DS	20/20	20/20	00	-1.0DS	20/20
4.	12year/M	20/125	0.8	-4DS	20/25	20/20	00	-	20/20
5.	12year/M	20/80	0.6	-3DS	20/20	20/20	00	-0.75DS	20/20
6.	17year/F	20/200	1.0	-5.25DS	20/25	20/20	00	-	20/20
7.	15year/F	20/63	0.5	-3.50DS	20/20	20/20	00	-0.5DS	20/20
8.	12year/F	20/125	0.8	-3.50DS	20/20	20/20	00	-1.00DS	20/20
9.	19year/M	20/200	1.0	-5DS	20/20	20/20	00	-0.75DS	20/20
10.	16year/F	20/200	1.0	-6.25DS	20/25	20/20	00	-0.50DS	20/20
11.	13year/M	20/80	0.6	-3.25DS	20/20	20/20	00	-1.75DS	20/20
12.	28year/F#	20/200	1.0	-6.25DS	20/80	20/20	00	-1.50DS	20/20
13.	20year/F	20/80	0.6	-4.50DS	20/20	20/25	0.1	-1.25DS	20/20
14.	14year/M	20/80	0.6	-3.25DS	20/20	20/20	00	-1.50DS	20/20
15.	16year/F	20/125	0.8	-4.50DS	20/20	20/20	00	-	20/20
16.	20year/M	20/400	02	-6.25DS	20/25	20/20	00	-1DS	20/20
17.	30year/#	20/400	02	-9.50DS	20/80	20/63	0.5	-7.50DS	20/25

[Table/Fig-4]: Clinical characteristics of patients with Anisomyopia

* Spherical equivalent, # did not fulfill our criteria of successful treatment

DISCUSSION

It has been suggested in the past, that treatment should be given to amblyopic patients even after the critical period [13]. In recent years a number of studies have shown that occlusion therapy is effective in older children as well [14-16]. Evidence has been accumulating

regarding neuronal plasticity of adult brain through experimental studies on animal models [17] and clinical trials using video games [18] or by employing perceptual learning technique [19]. Brar et al., [20] in their study on older amblyopic children have successfully reported use of full-time occlusion. The present study also shows

that it is possible to improve visual acuity of older anisometropic amblyopes, though we used occlusion time of 2-4 hours along with near work task. In our study, a success rate of 54% was observed if 20/20 BCVA was taken into account. This success rate increased to 77% if cut-off BCVA was taken as 20/25. If compared with earlier study of Patwardhan et al., [21] on patients of >12 years of age where they reported 60.7% success with BCVA of 20/40, our study shows a success rate of 95%. In PEDIG, 27% of patients between 10-18 years reported improvement of two or more lines with part-time occlusion [22]. Our study had a better success rate perhaps because counseling was given importance where poor compliance was suspected at each visit. Also, stress was given to near visual task in the form of video games, mobile phone gaming, hand writing and colouring using bright colours in special intricate and fine designs. Homework tracking and flexi-timings further resulted in better compliance. Since older children show poor compliance to patching, which is an important factor for the outcome of results, reducing the hours of patching can improve the compliance [23,24]. By decreasing the occlusion time from all waking hours to 2-4 hours/day and flexi-hours, compliance increases as seen in the successful results (54% success rate) in present study. This again is helpful in overcoming amblyopia in adults as it is very difficult to convince the older patients for occlusion all through the waking hours without hindering their routine work.

Although our study included patients of older age group (12-30years), the results are consistent with Paediatric Eye Disease Investigator Group study (PEDIG) where it was shown that in patients aged 7-17 years, decreasing the patching time for two to six hours daily, the response to amblyopia treatment increased to 53% [6].

The present study also highlights the importance of patching combined with near visual task, in the reversal of amblyopia [25]. Patients in which the therapy failed to produce the desired results had poor treatment compliance or perhaps there were other factors responsible. The answers to these questions need to be explored further.

Although there are limitations to this study due to small sample size and shorter follow up time, the present study certainly suggests a role of minimal occlusion therapy of 2-4 hours with stress on near visual task in all anisometropic amblyopic patients irrespective of age. It further shows that it is possible to treat amblyopia even after the critical period although it requires more effort on the part of patient and the care giver. Frequent follow-ups should be done to monitor progress. Successful cost-effective amblyopia treatment not only provides visual rehabilitation but also improves the quality of life as well as self-confidence of the patient and decreases the economic load on the government [26].

CONCLUSION

With mounting evidence of adult brain plasticity, perceptual learning, effect on visual performance by vision training exercises and significant results, (as seen in our study- 54% had BCVA of 20/20), it is important that all anisometropic amblyopic patients should be

treated with minimal 2-4 hours of occlusion or patching of better eye. This was a small study group, to fully explore the effects of occlusion therapy in adult anisometropic amblyope a long-term follow up and a large-scale study is required.

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PARTICULARS OF CONTRIBUTORS:

1. Assistant Professor, Department of Ophthalmology, Hamdard Institute of Medical Sciences and Research, Jamia Hamdard, New Delhi, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr, Taskin Khan,
Assistant Professor, Department of Ophthalmology, Hamdard Institute of Medical Sciences and Research,
Jamia Hamdard, New Delhi-110062, India.
Email: sarakhkhan2207@gmail.com

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