Evaluation of interactive binocular treatment in amblyopia

Samar A El-shayeb[1], Rasha M El-Zeini[2], Manal Ali kasem[2], Taher M Gamal[2].

[1]Ophthalmic Hospital, Mansoura, Egypt

[2]Ophthalmic Center, Faculty of Medicine, Mansoura University, Mansoura, Egypt

Corresponding author: Samar A El-shayeb Ophthalmology department, Faculty of Medicine, Mansoura University, Egypt. PO. 35516. Tel. 00201018711992. E-mail: s_a_942016@yahoo.com

Received: 23-11-2021, Accepted:28-2-2022 , Published online:16-3-2022

EJO(MOC) 2022;2:29-35.

Short title: Evaluation of interactive binocular treatment in amblyopia Abstract:

Abstract:

Purpose: This study was to evaluate effectiveness of I-BiT system for treatment of amblyopia in comparison with standard patching of dominant eye.

Methods: This was a prospective randomized comparative study conducted on cooperative amblyopic patients up to 20 years attending outpatient clinic of Mansoura University, Ophthalmic Center. All cases were exposed to full history taking, ophthalmic history, ocular examination which included assessment of visual acuity, slit lamp biomicroscopy, in addition to, Worth 4 Dot Test and Lang test.

Results: there was a statistically significant improvement in the (BCVA) ($p < 0.001$) of both groups after 6 months of treatment. There was a statistically significant improvement of Worth 4 dot test results with increased fusion in the cases of both groups. There was a statistically significant improvement of Lang test and achieving positive results in the cases of group 1(29.4% of cases) and group 2 (10.5% of cases) at 6 months of treatment as compared with the pretreatment data.

Conclusion: I-BiT system can give equal results to patching of sound eye in treating cases of moderate amblyopia but in a new, simple and joyful way.

Keywords: Amblyopia, interactive binocular treatment, binocular fusion.

INTRODUCTION:

Amblyopia is defined as unilateral or bilateral decreased best corrected visual acuity with no ocular pathologic or anatomic concerns[1]. Amblyopia prevalence is varied from 0.5% to 3.7% based on different epidemiological reports[2]. Amblyopia could be mild (6/9 - 6/15), moderate (6/15 - 6/30),or severe (worse than 6/30)[1].

Although various therapies have been suggested for treatment of amblyopia, patching of the dominant eye was recommended as a gold standard modality of amblyopia treatment. Lower compliance of children, necessity of long-term patching, and also lower rate of success in severe amblyopic cases can be considered some drawbacks of ocular patching. In addition, occlusion of one eye causes disruption of binocular fusion, and strabismus may be manifested consequently[3].

Therefore, an updated modality of amblyopia therapy which is named interactive binocular treatment has been introduced based on different mechanisms of[4]:

Using falling-blocks videogames that requires blocks moving down the screen to be tessellated together, videogame can be played using a pair of video goggles that allow for separate images to be presented to each eye or on a tablet computer device with red/blue anaglyph glasses. Neither eye sees all the game elements and, therefore, binocular combination is required for successful game play[5].

One of the advantages of I-BiT™ system is possibility of adjusting its illumination and image contrast according

to patient's BCVA, and it is effective even in individuals aged beyond limitation of amblyopia therapy[3].

Previous studies have revealed that I-BiT system can be beneficial as complementary treatment of patching and no manifestations of amblyopia recurrence was noted after one month following cessation of treatment[6].

PATIENTS & MOTHED:

This was a prospective randomized comparative study. It was carried out at Mansoura university, ophthalmic center, Egypt and was conducted in the period from January 2020 to December 2020. The study included total number of 40 patients with amblyopia that was divided into two groups, Group 1 included 20 patients who had eye patching for sound eye and Group 2 included 20 patients with I-BiT without patching.

This study included cooperative patients up to 20 years from both sexes and had unilateral moderate amblyopia with visual acuity (6/15: 6/30), excluding patients with mild and deep amblyopia, uncooperative patients, patients with previous therapy for amblyopia, patients with any untreated organic cause of amblyopia and patients with lack of follow up data for at least 3 months. A written informed consent was obtained from all the participants or their parents before inclusion in the study.

Methodology:

All patients were subjected to history taking in the form of general history as demographic data (age, sex and residency), their complaints with their medical and family history, also ophthalmic history that include history of wearing glasses, previous therapy for amblyopia, previous ocular trauma, previous ocular surgery and previous treatment for ROP.

The patient's external appearance was examined to detect any pathology like ptosis and visual acuity was assessed by using computerized visual acuity testing system and then transformed for statistical analysis to logarithm of minimal angle of resolution units (Log MAR). Objective refraction was done using autorefractometer followed by subjective refraction with trial frame and computerized visual acuity testing system.

This study used slit lamp biomicroscopy to assess anterior segment, Tono-pen tonometer to measure intraocular tension and indirect ophthalmoscope to assess posterior segment.

It also used Worth 4 Dot Test (distant type) and Lang test to evaluate binocular vision, fusion and stereopsis.

This study divided the patients randomly into 2 groups, group 1 used patching of better eye for two hours daily by an opaque adhesive patch while wearing their glasses and instructed to perform activities like doing homework or painting which motivates interaction between hands, eye and brain. While group 2 had I-BiT system without patching for 2 hours daily using red blue anaglyph glasses and specific mobile application (Amblyo mobile) at the normal reading distance (33 cm).

Patients were followed up for 6 months duration with assessment of best corrected visual acuity and grades of binocular vision at 2,4 and 6 months.

Statistical analysis of data:

The collected data were coded, processed and analyzed using the (Statistical Package for Social Sciences) version 22 for Windows® (IBM SPSS Inc). Qualitative data were expressed as number (percentage) within group and comparison between two groups of categorical data was conducted by using chi-square test. The used tests were Chi-square test, Monte Carlo correction, Student t-test, Fischer Exact test, and Mann Whitney test. For all the mentioned tests, the level of significance was tested, expressed as the probability of (p-value) and the results were explained as non-significant if the p value is > 0.05, as Significant if the p value is ≤ 0.05 and as highly significant if the p value < 0.001.

RESULTS:

In this study the mean age of the cases in group 1 was 9.57+/- 3.48 years and in group 2 was 11.50+/- 4.37 years, with no statistically significant difference between both (p=0.132). There was no statistically significant difference regarding sex between the two groups (p=0.744). anisometropia was seen in 80% of cases in group 1 and 90% of cases in group 2 with no statistically significant difference between the two groups (p=0.661) (table 1).

Table (1): Characteristics of the studied groups.

	Group 1	Group 2	Test of significance
Age/years			t=1.54
Mean ±SD	9.57±3.48	11.50±4.37	p=0.132
Sex	N=20	N=20	
Male	7(35.0)	8(40.0)	χ^2=0.107
Female	13(65.0)	12(60.0)	p=0.744
Types of amblyopia			
Anisometropic	16(80.0%)	18(90.0%)	
Strabismic	3(15%)	2(10.0%)	Fischer
Visual deprivation	1(5%)		exact test P=0.661

There was no statistically significant difference in the refractive state between group1 and group 2 amblyopic eyes, but higher prevalence of hypermetropia among study groups representing 80% of cases in group 1 (mean 2.55+/- 1.691) and 55% of cases in group 2 (mean 3.90 +/- 2.515) was noticed. (table 2).

Table (2): analysis of refractive state of studied groups

Refraction (Spherical equivalent)	Group 1 amblyopic eye n=20	Group 2 amblyopic eye n=20	between group1& group 2 amblyopic eye
Hypermetropic	16(80.0%)	11(55.0%)	P=0.091
Mean ±SD	2.55±1.691	3.90±2.515	
Myopic	4(20.0%)	9(45.0%)	
Mean ±SD	-8.50±4.999	-4.53±3.185	

BCVA improved significantly in amblyopic eyes of both groups after six-month of treatment (P < 0.001), while in comparison with each other, there was not any difference between them along the duration of the follow up. (figure 1).

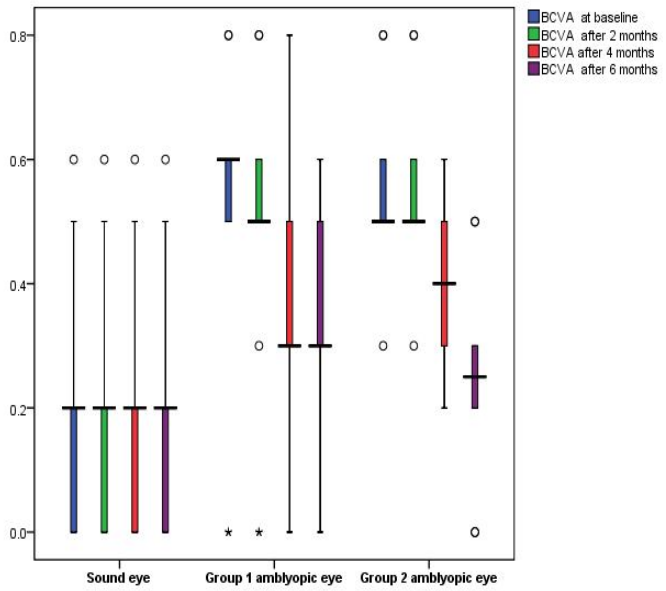

Figure (1): Comparison of BCVA between studied groups pre & post treatment.

There was a statistically significant improvement of Worth 4 dot test results in group1 (p=0.004) and in group 2(p=0.002) after 6 months of treatment in comparison to pretreatment data, but in overall there was no statistically significant difference between the cases in the two groups after 2, 4 and 6 months of treatment (table 3).

Table (3): analysis of Worth 4 dot test results between studied groups pre & post treatment.

Worth 4 dot test	Group 1	Group 2	Test of significance
Pre-treatment	N=20	N=20	
Fusion	6(30.0%)	5(25.0%)	χ^2=0.125
Suppression	14(70.0%)	15(75.0%)	p=0.723
After 2 months	N=20	N=20	
Fusion	8(40.0%)	6(30.0%)	χ^2=0.440
Suppression	12(60.0%)	14(70.0%)	p=0.507
After 4 months	N=17	N=20	
Fusion	11(64.7%)	10(50.0%)	χ^2=0.810
Suppression	6(35.3%)	10(50.0%)	p=0.368
After 6 months	N=17	N=19	
Fusion	14(82.4%)	15(78.9%)	FET
Suppression	3(17.6%)	4(21.1%)	P=1.0
Comparison between pre and post treatment	P2=0.50 P4=0.031* P6=0.004*	P2=1.0 P4=0.062 P6=0.002*	

P2: difference between pre-treatment and after 2 months of follow up, P4: difference between pre-treatment &

after 4 months, P6: difference between pre-treatment and 6 months after treatment. FET: Fischer exact test, χ^2=Chi-Square test

Although stereopsis improved in group 1 (P < 0.025) and group 2 (P < 0.025) after 4 months of treatment, there was no significant difference between them pre- and post-therapy. The percentage of cases with doubtful Lang results increased in the two groups along the study period. positive results in the cases of group 1 (29.4% of cases) and group 2 (10.5% of cases) appeared after 6 months of treatment. (table 4).

Table (4): Analysis of lang test results between studied groups pre & post treatment.

Lang test	Group 1	Group 2	Test of significance
Pre-treatment	N=20	N=20	
	14(70.0%)	19(95.0%)	χ^2 =4.33
-ve	6(30.0%)	1(5.0%)	p=0.037*
Doubtful			
After 2 months	N=20	N=20	
	14(70%)	19(95.0%)	FET
-ve	6(30.0%)	1(5.0%)	P=0.091
Doubtful			
After 4 months	N=17	N=20	
	7(41.2%)	14(70.0%)	χ^2 =3.11
-ve	10(58.8%)	6(30.0%)	p=0.078
Doubtful			
After 6 months	N=17	N=19	
	5(29.4%)	2(10.5%)	
+ve	3(17.6%)	8(42.1%)	MC
-ve	9(52.9%)	9(47.4%)	P=0.177
Doubtful			
Comparison between pre and post treatment	P2=1.0	P2=1.0	
	P4=0.025*	P4=0.025*	
	P6=0.741	P6=0.109	

P2: difference between pre-treatment and after 2 months of follow up, P4: difference between pre-treatment & after 4 months, P6: difference between pre-treatment and 6 months after treatment.

MC: Monte Carlo test, χ^2=Chi-Square test

DISCUSSION:

Amblyopia is a decrease in BCVA that can be treated if there is no structural pathology. It might be unilateral or bilateral[7]. optimal management of amblyopia is one of the primary challenges in pediatric ophthalmology research[8].

The use of an eye patch to treat amblyopia in children has been demonstrated to be helpful, but distressing for the kid and has a detrimental influence on school and home life. Patching treatment compliance is generally poor, resulting in sub-optimal treatment outcomes[9]. Penalization, most typically with atropine, is the principal alternative to patching that is routinely utilized. Patching and penalization have variable results and take a long time to work[10,11].

To treat amblyopia, the Interactive Binocular Treatment project was initiated. The idea was that amblyopia was a binocular issue that required a binocular solution, which dichoptic training can provide[12]. The I-BiT technology allowed both eyes to see an image, but only the amblyopic eye could see key elements of the image[13].

There are limited number of studies that reveal the value of the Interactive Binocular Treatment in management of amblyopia especially here in Egypt. so, this study was conducted in Mansoura University Ophthalmic center to evaluate effectiveness of I-BiT system for treatment of amblyopia in comparison with standard patching of dominant eye. Theis study included 40 patients who were randomly classified into 2 groups; group 1 that included 20 patients who were treated with eye patching for sound eye and group 2 that included 20 patients who were treated with I-BIT system without patching.

In this study, the mean age of the cases in group 1 was 9.57+/- 3.48 years and the mean age in group 2 was 11.50+/- 4.37 years, with no statistically significant difference between the two groups (p=0.132).

Yao et al. (2020)[14] found that the mean age at treatment was 5.92+/- 2.61 years in the binocular group against 5.68+/- 2.26 years in the patching group, with no statistically significant difference between the two groups (p= 0.72). Rajavi et al. (2019)[3] evaluated 38 unilateral amblyopic patients with a mean age of 7.08 1.82 years in both the case (6.5+/- 2.01 years) and control (7.55+/- 1.55

years) groups , there was no difference between the two groups.

In this study, there were 35% boys and 65% girls in group 1 while in group 2, there were 40% boys and 60% girls. there was no statistically significant difference regarding sex between the two groups (p=0.744). This was in agreement with Rajavi et al. (2016)[15].

In this study, there was no statistically significant difference in the refractive state between two study groups of amblyopic eyes (p=0.091). There was higher prevalence of hypermetropia among study groups representing 80% of cases in group 1 and 55% of cases in group 2.

This was in accordance with Yao et al. (2020)[14] who found no statistically significant variation in refractive status across cases in the research groups (p=0.47). In both study groups, hyperopic eyes accounted for the largest percentage.

In this study, there was a statistically significant improvement in the BCVA (p <0.001) after 6 months of treatment in group 1 and group 2 amblyopic eyes, however there was no statistically significant difference in the BCVA between the cases of the 2 groups along the duration of follow up.

This study results matched those of Rajavi et al. (2019)[3] who found that I-BiT treatment resulted in an equivalent improvement in BCVA during a one-month treatment period when compared to patching with a placebo game.

Binocular therapy produced more strong VA improvements in patients with amblyopia, which is consistent with our findings[16].

This study's findings partially coincided with Rajavi et al. (2016)[15], who found that there was a significant difference in BCVA between the two groups after one month of treatment (p< 0.001), however there was no significant change in BCVA between the two groups at the end of the second month of treatment (p = 0.246).

Kelly et al. (2016)[17] employed the identical Dig Rush binocular game and found that cases treated with 2 weeks of binocular therapy improved more than controls treated with part-time patching.

This study findings, on the other hand, contradicted those of Holmes et al. (2016)[18], Yao et al. (2020)[14] and Manh et al. (2018)[19] who found a statistically significant difference in the VA, with the patching group showing more improvement

In this study, we used Worth 4 dot test to assess improvement of fusion ability with treatment and the study concluded that there was a statistically significant improvement of Worth 4 dot test results in the cases of group 1, at 4 months and 6 months as compared with the pretreatment data. in group 2, there was a statistically significant improvement of Worth 4 dot test results only at 6 months as compared with the pretreatment data, but with no significant difference between the 2 groups.

These findings contradicted those of Li et al.,2014[4], who found no significant change in the intensity of suppression. Knox et al. (2012)[20] reported similar findings.

This study used lang test for assessment of near stereoacuity and found that there was no statistically significant difference in the lang test results between the cases in the two groups after 2, 4 and 6 months of treatment. There was a statistically significant improvement of Lang test results in the cases of group 1 and group 2 at 6 months as compared with the pretreatment data.

This was in accordance with Rajavi and his colleagues (2019)[3]. Despite the fact that they used the Titmus stereoacuity test, they found the same results in both cases (P = 0.001) and controls (P = 0.001). This is in contrast to Kelly et al. (2016)[17], who found no difference in stereoacuity with the binocular game or patching after a 2-week visit. This is primarily owing to the treatment's short duration and lack of longer follow-up.

This study used amore simplified technique of I-BiT system with red-blue anaglyph glasses and mobile application (Amblyo mobile) allowing for easy daily at home training and completed follow up for 6months.

Rajavi et al.,2019[3] used I-BiT™ software, in which the dominant eye sees the fixed target while the amblyopic eye follows the moving object through red and green filters, but for a shorter period of time (1 month) and found the same results. Unlike earlier trials that used a more

complicated I-BiT system, which required patients to visit the orthoptic clinic once a week for 30 minutes of I-BiT treatment for six weeks, for a total treatment time of three hours[9].

Conclusion:

I-BiT system can give equal results to patching of sound eye in treating cases of moderate amblyopia considering improvement of BCVA, fusion and stereopsis. Unlike patching, I-BiT system offers a new, simple and joyful way of treating amblyopia with no psychological impact on patients or parents.

Availability of data and materials: All the data supporting our findings is contained within the manuscript.

ACKNOWLEDGEMENT: None

Corresponding author

Correspondence to: Sally G. Emarah

Email: sallyemarah@hotmail.com

Affiliations

Sally G. Emarah, Mansoura University, Egypt.

Ethics declarations

Conflict of interest

Sally G. Emarah, Eman Azmy, Walid Abu Samra, Mohammad Khalaf all authors have no conflicts of interest that are directly relevant to the content of this review.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial or not for profit sectors.

Reviewer disclosures: No relevant financial or other relationships to disclose.

Declaration of interest: No financial affiliations or financial involvement with any organization or entity with a financial competing with the subject matter or materials discussed in the review

References:

1. Rajavi Z, Sabbaghi H, Baghini AS, Yaseri M, Moein H, Akbarian S, et al. Prevalence of amblyopia and refractive errors among primary school children. Journal of ophthalmic & vision research. 2015;10:408.
2. Hashemi H, Pakzad R, Yekta A, Bostamzad P, Aghamirsalim M, Sardari S, et al. Global and regional estimates of prevalence of amblyopia: A systematic review and meta-analysis. Strabismus. 2018;26:168-83.
3. Rajavi Z, Sabbaghi H, Sharifi EA, Behradfar N, Kheiri B. Comparison between patching and interactive binocular treatment in amblyopia: a randomized clinical trial. Journal of current ophthalmology. 2019;31(4):426-31.
4. Li SL, Jost R, Morale S, Stager D, Dao L, Stager D, et al. A binocular iPad treatment for amblyopic children. Eye. 2014;28(10):1246-53.
5. Hess RF, Babu RJ, Clavagnier S, Black J, Bobier W, Thompson B. The iPod binocular home-based treatment for amblyopia in adults: efficacy and compliance. Clinical and Experimental Optometry. 2014;97(5):389-98.
6. Mezad-Koursh D, Rosenblatt A, Newman H, Stolovitch C. Home use of binocular dichoptic video content device for treatment of amblyopia: a pilot study. Journal of American Association for Pediatric Ophthalmology and Strabismus. 2018;22(2):134-8. e4.
7. Rashad MA, Abd Elaziz KM, Fawzy SM. Screening of primary school children for amblyopia and Amblyogenic factors in central Cairo, Egypt. Journal of ophthalmology. 2018;2018.
8. Lamprogiannis L, MacKeith D, Vivian AJ. A Review of Binocular Treatment for Amblyopia. 2020.
9. Herbison N, Cobb S, Gregson R, Ash I, Eastgate R, Purdy J, et al. Interactive binocular treatment (I-BiT) for amblyopia: results of a pilot study of 3D shutter glasses system. Eye. 2013;27(9):1077-83.
10. Awan M, Proudlock F, Grosvenor D, Choudhuri I, Sarvananthan N, Gottlob I. An audit of the outcome of amblyopia treatment: a retrospective analysis of 322 children. British Journal of Ophthalmology. 2010;94(8):1007-11.
11. Newsham D, Amenos MC. Recent advances in the management of amblyopia. Optometry. 2011;12(3):119-28.

12. Pineles SL, Aakalu VK, Hutchinson AK, Galvin JA, Heidary G, Binenbaum G, et al. Binocular treatment of amblyopia: a report by the American academy of ophthalmology. Ophthalmology. 2020;127(2):261-72.
13. Falcone MM, Hunter DG, Gaier ED, editors. Emerging therapies for amblyopia. Seminars in Ophthalmology; 2021: Taylor & Francis.
14. Yao J, Moon H-W, Qu X. Binocular game versus part-time patching for treatment of anisometropic amblyopia in Chinese children: a randomised clinical trial. British Journal of Ophthalmology. 2020;104(3):369-75.
15. Rajavi Z, Sabbaghi H, Sharifi EA, Behradfar N, Yaseri M. The role of interactive binocular treatment system in amblyopia therapy. Journal of current ophthalmology. 2016;28(4):217-22.
16. Hess RF, Thompson B. Amblyopia and the binocular approach to its therapy. Vision research. 2015;114:4-16.
17. Kelly KR, Jost RM, Dao L, Beauchamp CL, Leffler JN, Birch EE. Binocular iPad game vs patching for treatment of amblyopia in children: a randomized clinical trial. JAMA ophthalmology. 2016;134(12):1402-8.
18. Holmes JM, Manh VM, Lazar EL, Beck RW, Birch EE, Kraker RT, et al. Effect of a binocular iPad game vs part-time patching in children aged 5 to 12 years with amblyopia: a randomized clinical trial. JAMA ophthalmology. 2016;134(12):1391-400.
19. Manh VM, Holmes JM, Lazar EL, Kraker RT, Wallace DK, Kulp MT, et al. A randomized trial of a binocular iPad game versus part-time patching in children aged 13 to 16 years with amblyopia. American journal of ophthalmology. 2018;186:104-15.
20. Knox PJ, Simmers AJ, Gray LS, Cleary M. An exploratory study: prolonged periods of binocular stimulation can provide an effective treatment for childhood amblyopia. Investigative ophthalmology & visual science. 2012;53(2):817-24.