

Comparison of the effectiveness of amblyopia treatment with eye-patch and binocular Occlu-tab for the same treatment duration

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Purpose: This study aimed to compare the conventional eye patch with Occlu-tab—a binocular open-type amblyopia training device—and evaluate their effectiveness in amblyopia treatment. **Methods:** In this prospective, multi-center study, 40 patients between ages 3 to 12 years, diagnosed with anisometropic amblyopia (refraction difference of both eyes ≥ 2 D, best-corrected visual acuity [BCVA] of the amblyopic eye ≤ 0.1 [logMAR]) were treated with Occlu-tab or conventional eye patch for 1 h per day thrice a week. We compared the visual acuity of both groups before and after 6, 7, and 8 weeks of amblyopia treatment. One-way repeated-measures analysis of variance and Tukey's test were used to compare the visual acuity of both groups pre- and post-treatment. **Results:** Both groups had significantly improved visual acuity at 6, 7, and 8 weeks compared to that before treatment (all $P < 0.001$). The improvement in BCVA of the Occlu-tab group (0.33 ± 0.25) was significantly greater than that of the eye patch group (0.16 ± 0.17) after 8 weeks of treatment ($P = 0.02$). **Conclusion:** Amblyopia treatment using binocular open game training with Occlu-tab led to greater improvement in visual acuity than that with a conventional eye patch for the same treatment duration.

Key words: Amblyopia, anisometric amblyopia, eye patch, game-based treatment, Occlu-tab, visual acuity

Amblyopia occurs in approximately 1%–5% of children. It impairs the development of visual function, and severe cases of amblyopia can interfere with school and social life.^[1–4] Many children with amblyopia receive occlusion therapy (eye patch treatment), the gold-standard treatment modality for amblyopia.^[5–7] However, one of the pitfalls of treating amblyopia with an eye patch is low treatment compliance due to non-psychosocial (i.e., the age at treatment and severity of amblyopia) and psychosocial (i.e., lack of knowledge about amblyopia and treatment, stress, and lack of motivation) causes.^[8] Perhaps, due to these issues, a new game-based amblyopia treatment has been reported in recent years.^[9–12] In pediatric patients capable of playing games, better compliance can be expected with game-based amblyopia treatment than with eye patch treatment.^[12]

Recently, we presented a method and device (Occlu-tab, also known as Occlu-pad in Japan) for amblyopia treatment involving the use of open binoculars with a modified common tablet device.^[13–15] The Occlu-tab has three key functions.

First, the white-screen technology eliminates the side effects of conventional eye patches and enhances stimulation of the visual field by selectively presenting images to one eye while both eyes are open. Second, it can automatically record the actual treatment time and thus accurately evaluate the treatment duration. Third, it provides a game therapy by using a palm-sized block (when pediatric patients grab any side of the block, the body is electrically coupled to the block) called the Tangi block. In a randomized clinical trial by Iwata *et al.*,^[15] the addition of Occlu-tab treatment to refractive correction (glasses) resulted in a significant improvement in visual acuity compared to that by wearing glasses alone. Moreover, we reported that the improvement in visual acuity and adherence to Occlu-tab treatment was notably higher for both strabismic amblyopia and anisometropic amblyopia when compared with the amblyopia treatment effect of the eye patch. However, in previous studies, due to differences in treatment compliance, the reported treatment duration for the eye patch and Occlu-tab were not the same.^[14] Therefore, the treatment effect of each method with the same treatment duration has not yet been evaluated. In this study, we investigated the effectiveness of amblyopia treatment with the eye patch and binocular Occlu-tab for the same treatment duration.

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Cite this article as: Handa T, Thakkar H, Ramakrishnan M, Shah K, Prajapati V, Sayed S, *et al.* Comparison of the effectiveness of amblyopia treatment with eye-patch and binocular Occlu-tab for the same treatment duration. *Indian J Ophthalmol* 2022;70:1722-6.

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Received: 27-Jun-2021

Revision: 10-Oct-2021

Accepted: 17-Dec-2021

Published: 28-Apr-2022

Access this article online

Website:

www.ijo.in

DOI:

10.4103/ijo.IJO_1733_21

Quick Response Code:



Methods

Study population

This randomized controlled clinical trial complied with the tenets of the Declaration of Helsinki and was approved by the institutional ethics committees of two medical hospitals (approval no.: 92/2018 and 09/04/2018). The aim and potential outcomes of the study were thoroughly explained to all participants and guardians who then provided informed consent.

This study included patients who presented to the hospital for the first time and were diagnosed with anisometropic amblyopia (refraction difference of both eyes ≥ 2 D; highest visual acuity of the amblyopic eye ≤ 0.1 [logMAR], using Snellen chart by ophthalmologist and optometrist), were aged 3- to 12- years old, and had visited the clinic three times a week for 8 weeks (2 months) after the start of amblyopia treatment. Patients were excluded if they had a history of amblyopia treatment, were diagnosed with strabismus, had difficulty in completing the visual acuity or refraction examination, or were receiving occlusion therapy using an eye patch.

Occlu-tab

Occlu-tab presents target images on an invisible tablet terminal to only the amblyopic eye with a binocular open view [Fig. 1a]. The invisible display has a quarter-wave plate marked on a polarizing film layer, which is altered by a linear polarization filter on a liquid crystal display. The output image of Occlu-tab cannot be seen by the naked eye because humans cannot natively perceive polarization. However, it is possible to see an image on the invisible display through a polarization filter. Patients wear specially designed polarization glasses, as shown in Fig. 1. The amblyopic eye can see the original image through a circular polarization filter even if the tablet is rotated or the patient tilts their head. In contrast, the healthy eye cannot see the original image because a light reduction filter is applied. The optical density of the light reduction filter and polarization filter are the same.

Occlu-tab has the advantage of being portable, full color, touchscreen-based, and user-friendly with a tangible block

for eye-hand coordination. Occlu-tab has the following eight training eye-hand coordination training games, which use the Tangi block [Fig. 2]: 1. Sheep shearing, 2. Window cleaning, 3. Whack-a-mole, 4. Animal catching, 5. Egg race, 6. Ball juggling, 7. Alien hunter, and 8. Capsule toys and collection.

Power calculations and randomization

In this randomized controlled trial, randomization was based on a permuted block method, which was performed using random numbers generated in Microsoft Excel, with a 2-block size. The difference in visual acuity (logMAR) between groups was estimated as 0.1 ± 0.1 based on a previous study.^[15] For $\alpha = 0.05$ and a power of 0.8, the required sample size was 17 children per group. Anticipating a 10% dropout rate, we enrolled 40 pediatric patients (20 per group).

Treatment methodology

Forty children diagnosed with anisometropic amblyopia (mean age \pm standard deviation: 8.2 ± 2.2 years) were recruited. All patients wore complete correction glasses fitted with cycloplegic refraction. Twenty patients were treated for amblyopia with an eye patch ("eye-patch treatment group": 7.8 ± 2.2 years of age), whereas the other 20 patients were treated with Occlu-tab ("Occlu-tab treatment group": 8.7 ± 2.2 years of age). In the eye-patch treatment group, the doctor instructed the amblyopic pediatric patients and their guardians to visit the eye clinic 3 days a week and to train using the eye patch for 60 min during each visit, although 3 h of treatment in a week for conventional eye-patch treatment is rare. Training for the eye-patch treatment group included coloring, writing letters, and watching animations on a monitor [Fig. 1b]. In the Occlu-tab treatment group, the doctor instructed the amblyopic pediatric patients and their guardians to visit the clinic 3 days a week and to train with Occlu-tab for 60 min during each visit. The Occlu-tab treatment was delivered as an eye-hand coordination training game [Fig. 1c]. Ophthalmology staff (usually an optometrist) who was not part of this study confirmed whether the child was being trained properly during the treatment with the eye patch or Occlu-tab.

Statistical analysis

One-way repeated-measures analysis of variance (One-way RM ANOVA) and Tukey's test were used to compare visual acuity before and after treatment with the eye patch and Occlu-tab. The *t* test was used to compare the improvement in visual acuity between the eye patch treatment group and the Occlu-tab treatment group. *P* < 0.05 was considered statistically significant. Statistical analysis was performed using SigmaPlot (version 12.5, Systat Software, Inc.).

Results

BCVA (logMAR) differences between the healthy and amblyopic eye were 0.61 ± 0.28 in the eye patch treatment group versus 0.58 ± 0.32 in the Occlu-tab treatment group, whereas the refractive differences were 3.89 ± 1.64 D (-0.78 ± 2.17 D in the healthy eye: range +3.0 to -6.0 D, -1.96 ± 5.73 D in the amblyopic eye: range +5.5 to -10.0 D) in the eye-patch treatment group versus 4.13 ± 2.60 D (-0.20 ± 2.39 D in the healthy eye: range +5.0 to -8.0 D, -1.60 ± 6.28 D in the amblyopic eye: range +8.5 to -16.0 D) in the Occlu-tab treatment group.

Table 1: Best-corrected visual acuities before treatment and 1, 2, 3, 4, 5, 6, 7, and 8 weeks after the start of amblyopia treatment

	Eye-patch treatment	Occlu-Tab treatment
Before treatment	0.73±0.16	0.69±0.28
1 week	0.73±0.17 (<i>P</i> =1.00)	0.68±0.28 (<i>P</i> =1.00)
2 weeks	0.71±0.18 (<i>P</i> =0.99)	0.64±0.29 (<i>P</i> =0.97)
3 weeks	0.70±0.19 (<i>P</i> =0.95)	0.60±0.31 (<i>P</i> =0.39)
4 weeks	0.68±0.18 (<i>P</i> =0.59)	0.59±0.31 (<i>P</i> =0.30)
5 weeks	0.65±0.18 (<i>P</i> =0.07)	0.57±0.32 (<i>P</i> =0.10)
6 weeks	0.56±0.20 (<i>P</i> <0.001)	0.41±0.23 (<i>P</i> <0.001)
7 weeks	0.56±0.20 (<i>P</i> <0.001)	0.40±0.22 (<i>P</i> <0.001)
8 weeks	0.56±0.20 (<i>P</i> <0.001)	0.35±0.23 (<i>P</i> <0.001)

Best-corrected visual acuities at 6, 7, and 8 weeks after the start of eye-patch/Occlu-tab treatment significantly improved as compared to that before treatment (*P*<0.05, by One-way repeated-measures analysis of variance and Tukey's test)



Figure 1: Photographs of the treatment methods. The images depict the appearance of the Occlu-tab (a), eye-patch treatment (b), and Occlu-tab treatment (c). For the Occlu-tab treatment, the game can only be viewed through the right (amblyopic) eye. Both eyes can always see the user's fingers, Tangi block, and any object in the peripheral visual field, such as the edge of the tablet on the tabletop

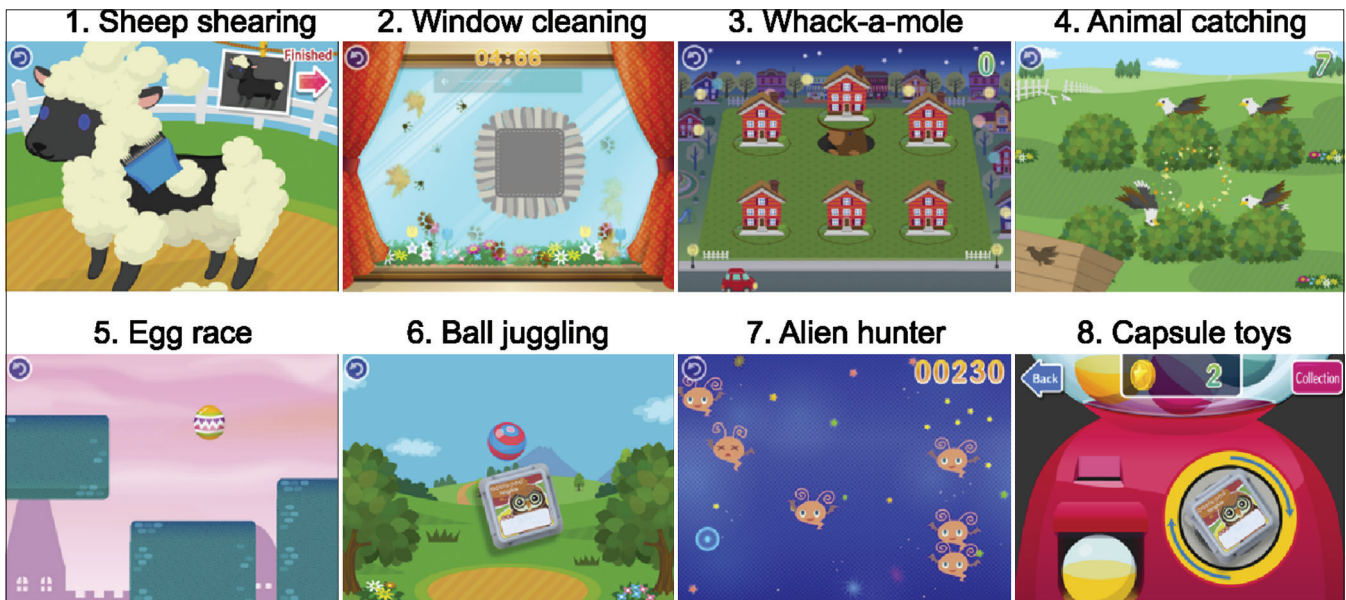


Figure 2: Games for the Occlu-tab. The eight games are designed to encourage quick and approximate eye-hand coordination with horizontal and vertical eye movements. The games are as follows: 1. Sheepshearing, wherein the Tangi block acts as an electric clipper and the goal is to cut the sheep's hair according to the prescribed shape; 2. Window cleaning, wherein the Tangi block acts as a dust mop and the goal is to clean the windows in a specified short time; 3. Whack-a-mole, wherein the Tangi block acts as a hammer and the goal is to hit all the moles, which appear quickly; 4. Animal catching, wherein the Tangi block acts as a net and the goal is to catch all the birds, which appear quickly; 5. Egg race, wherein the user carries the egg using the Tangi block in a horizontally scrolling world until reaching the goal; 6. Ball juggling, wherein the patient keeps juggling a ball using the Tangi block until the specified end time; 7. Alien hunter, wherein the patient defeats multiple aliens in a vertical scrolling world by operating a fireball by using the Tangi block; and 8. Capsule toys and collection (known as Gashapon in Japan), wherein the patient collects randomly appearing characters by rotating the lever of a Gashapon using the Tangi block

Both the eye-patch and Occlu-tab treatment groups exhibited improved visual acuity after treatment. The pretreatment BCVA of the eye patch and Occlu-tab groups were 0.73 ± 0.16 and 0.68 ± 0.28 logMAR, respectively; after 8 weeks of treatment, the BCVA were 0.56 ± 0.20 and 0.34 ± 0.23 logMAR, respectively [Table 1]. Both the eye-patch and Occlu-tab treatments significantly improved the BCVA after 6 weeks of treatment compared to the BCVA at the start of treatment ($P < 0.001$, One-way RM ANOVA and Tukey's test).

The improvements in the BCVA of the eye patch and Occlu-tab treatment groups were 0.16 ± 0.17 and 0.33 ± 0.25

logMAR after 8 weeks of treatment, respectively [Fig. 3]. There was a statistically significant increase in the improvement of BCVA in the Occlu-tab treatment group after 8 weeks of treatment ($P = 0.02$, t-test, $t = -2.30$, $df = 38$, 95%CI for difference: -0.316 to -0.0242 logMAR).

Discussion

In the present study, amblyopia treatment using Occlu-tab resulted in a better improvement in visual acuity than that with treatment using an eye patch. Although amblyopia training time was limited to only 3 h per week, a visual acuity

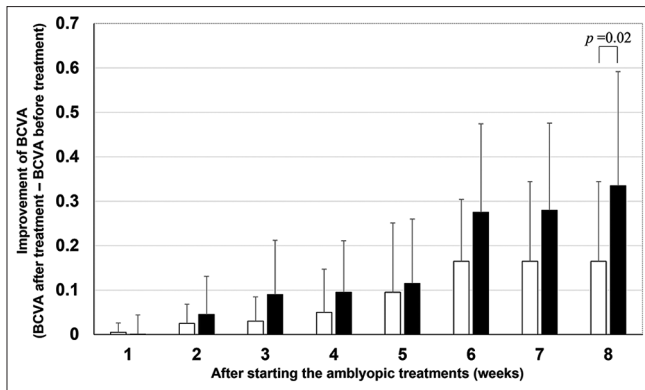


Figure 3: Improvement in visual acuity across 8 weeks of amblyopia treatment with an eye patch or Occlu-tab. White bars indicate the improvement in best-corrected visual acuities (BCVA, mean \pm standard deviation) with eye-patch treatment. Filled bars indicate the improvement in BCVA with Occlu-tab treatment. Improvement in BCVA significantly differed between the eye-patch and Occlu-tab groups after 8 weeks of treatment ($P = 0.02$ by t test)

improvement of 0.3 logMAR was observed at 8 weeks, which was significantly greater than that observed with the eye patch. Amblyopia treatment in this study was outpatient training. Compliance with the amblyopia treatment was 100% for both treatment modalities. Therefore, the difference in visual acuity improvement between the Occlu-tab and eye-patch groups in this study was due to the type of treatment, not due to a difference in treatment duration.

Conventional eye-patch treatment physically blocks the healthy eye to force the use of the amblyopic eye. In contrast, although Occlu-tab is a treatment method in which only the amblyopic eye is forced to be used despite both eyes being open, the frame and operation blocks of the tablet, which do not show the image, are seen by both eyes, and the peripheral fused image is maintained. Amblyopia is considered to involve strong cortical inhibition in the visual cortex^[16] and a blockage of neural connections from the amblyopic eye.^[17] Therefore, it is desirable to increase the level of activity in the visual cortex. Indeed, during game training with Occlu-tab, the bilateral activity of the occipital lobe of the visual cortex (measured by the change in oxygenated hemoglobin kinetics) has been found to be significantly greater than that observed with single-eye occlusion.^[18]

The most important aspect of the critical period of visual cortex development is the massive increase in neural connections during early infancy.^[19] These neural connections constantly change throughout early childhood, leading to the formation of correct connections and inhibition of incorrect connections.^[16,20] Whether a neural connection remains intact or is suppressed depends on whether that connection is used. The basic principle of amblyopia treatment involves forcing the use of neural connections associated with the amblyopic eye. The variety, intensity, and type of visual stimuli are especially important for brain development in children.^[16] In the present study, there was no age difference between the Occlu-tab and eye-patch groups, and the treatment duration and treatment environment were the same in both groups. There is a previous report of cognitive improvement with the use of games;^[21] however, the mechanism underlying the effect of games on cognitive improvement remains unclear. In contrast, the Occlu-tab

training game seems to contribute to the development of children's attention and cognition (especially in vision testing) through the combined sensory stimulation of observed-body coordination (eye-hand coordination). Rehabilitation using video games is an innovative tool that can increase motivation in pediatric patients.^[22]

The detection of amblyopia is likely to be delayed if there are insufficient ophthalmic examinations in childhood. When treating amblyopia after the general critical period, it is optimal to choose a method that is highly effective, has no side effects, and does not interfere with social life, such as school. The eye-patch method of occluding healthy eyes must be reconsidered in terms of the target age, effectiveness, and side effects. A major problem with eye-patch treatment is poor adherence;^[23,24] long and intensive eye-patch training is more likely to result in lower compliance in school-aged children than in preschool children due to psychosocial problems.^[25] The possibility of amblyopia training using video games (monocular and dichoptic) was recently reported.^[9-12] In children capable of playing the games, compliance with amblyopia treatment with such binocular games is better than amblyopia treatment with an eye patch. In a study of Japanese children (3–9 years old), compliance was significantly higher in the Occlu-tab treatment group than that in the eye-patch treatment group after 3 months of treatment.^[10] In addition, compliance in the Occlu-tab treatment group ranged from 68% to 72% throughout the entire treatment period. Therefore, we believe that game-based treatment methods are effective in maintaining high treatment compliance in pediatric amblyopia treatment.

The current study involved training for only 3 h per week in visiting the eye clinic; thus, the effects of home training for approximately 4 h daily in addition to training of visiting the eye clinic three times a week remains unknown. In addition, the study was limited to the treatment of anisometropic amblyopia; thus, the effect of treatment on strabismus amblyopia or other forms of amblyopia remains unknown. Future studies should consider strabismic amblyopia and other forms of amblyopia. Overall, our results indicate that Occlu-tab amblyopia training in Indian children was beneficial. However, to support worldwide dissemination of this approach, it will be necessary to analyze the effects of different types of games and clarify possible cultural and religion-related issues. Nevertheless, Occlu-tab treatment can become a viable option for pediatric amblyopia treatment in both developed and developing countries.

Conclusion

In conclusion, amblyopia treatment using Occlu-tab resulted in a better improvement in visual acuity than that with eye-patch treatment for the same treatment duration. Further studies will determine whether Occlu-tab can become the generally preferred treatment option for pediatric amblyopia.

Acknowledgements

We would like to thank Editage (www.editage.com) for English-language editing.

Financial support and sponsorship

This work was supported in part by the SDGs Business Verification Survey with the Private Sector for "Amblyopia

Treatment for Children in India" supported by JICA's SDGs Business Verification Survey with the Private Sector for "Amblyopia Treatment for Children in India"; by the Japan Prize Heisei Memorial Research Grant Program; and by the JSPS KAKENHI Grant Number 21K12196.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Conflicts of interest

There are no conflicts of interest.

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