〈Regular Article〉

Outcomes of binocular treatment using a Bangerter occlusion film and computer games in patients with intractable unilateral amblyopia

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ABSTRACT PURPOSE: To report outcomes following binocular treatment using a Bangerter occlusion filter (BF) and computer games in patients with intractable amblyopia.

METHODS: Eight patients (4 boys, mean ± SD age: 8.0 ± 0.8 years) with unilateral amblyopia that did not respond to conventional treatments were studied. They were instructed to play action games for one hour a day while wearing spectacles with an adequate level of BF in front of the non-amblyopic eye so that the visual input became the same between the two eyes. They continued this exercise for eight weeks, and we assessed their visual acuity and spatial sensitivity at baseline, and at 4- and 8-week visits. To confirm the maintenance of efficacy after the treatment, we assessed them again at a 12-week visit.

RESULTS: The mean log MAR at distance improved from 0.32 to 0.24 at the 4-week visit ($p < 0.05$), and appeared to continue up to eight weeks, but returned to the baseline level at the 12-week visit (four weeks after terminating the treatment). There was no significant improvement in the mean log MAR at near. Contrast sensitivity significantly improved only at three cycles/degree ($p < 0.05$), and this effect persisted until the 12-week visit. The distance log MAR at the 12-week visit had a significant correlation with the strength of suppression for the amblyopic eye at baseline ($r = 0.71$, $p < 0.05$).

CONCLUSIONS: Binocular treatment improved visual function only in terms of contrast sensitivity at low spatial frequency. Patients who have weak suppression may gain some benefit from this treatment.

doi：10.11482/KMJ-E202248017 *(Accepted on March 31, 2022)*

Key words：Binocular based treatment, Monocular amblyopia, Depth of suppression, Strabismic amblyopia, Microtropic amblyopia, Contrast sensitivity

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INTRODUCTION

Occlusion therapy is the gold standard for amblyopia treatment. However, compliance with this treatment is poor in some patients due to the need for prolonged application of an eyepatch to the non-amblyopic eye and/or appearance problems. In addition, there are concerns about form-deprivation amblyopia in the non-amblyopic eye and the adverse effects of strabismus due to binocularity dissociation. Penalization, blurring of the retinal image by applying cycloplegic eye drops to the non-amblyopic eye, is another treatment option and although it has been reported that the therapeutic effect is not significantly different from that of occlusion therapy[1)], there are problems such as photophobia and excessive exposure to ultraviolet radiation due to mydriasis and allergic reactions to the eye solution. It is not uncommon for children who cannot adapt to these treatments to abandon amblyopia treatment after the sensitive period for developing visual acuity (6-8 years of age).

It has been considered that visual information from the amblyopic eye is not combined with that from the non-amblyopic eye. However, several clinical studies reported that the combining mechanism is maintained even in amblyopic patients[2-4)]. The lack of binocular function sometimes observed in unilateral amblyopia is due to the unequal input of visual information from both eyes, and the strong inhibitory effect of the non-amblyopic eye on the amblyopic eye prevents the development of visual acuity. For this reason, binocular amblyopia treatment that equalizes the contrast of the retinal image between the two eyes has recently been the focus of attention[5-8)]. For example, a randomized clinical trial[6)] reported that the therapeutic effect was not different between a group undergoing binocular treatment with a Bangerter occlusion film (BF) and a group undergoing occlusion therapy for two hours a day. Another RCT comparing a group undergoing binocular treatment with a group using spectacles reported that the treatment period required to reach a level of visual acuity difference of 1 line or less between the eyes was significantly shorter in the former group[7)].

In this study, we applied binocular amblyopia treatment in combination with computer game tasks to patients with unilateral amblyopia that were difficult to treat with conventional amblyopia treatments and report the outcomes.

SUBJECTS AND METHODS

This study was conducted after obtaining approval from the Ethics Committee of Kawasaki Medical School (No. 2572).

Subjects

Patients with intractable unilateral amblyopia were included in this study. The inclusion and exclusion criteria are listed below. Eligibility was investigated and determined based on past medical records. The purpose of the study, expected events, and possible unfavorable events were explained to the children who met the eligibility criteria and their guardians, and written consent was obtained. The diagnosis included anisometropic amblyopia, microstrabismic amblyopia, and mixed amblyopia.

Inclusion criteria:

1) Adherence score[9)] to occlusion therapy in the past six months was poor or fair, or the adherence score to ophthalmic therapy alone or occlusion therapy with penalization was good or excellent, as well as improvement in visual acuity of 0.1 log MAR or less.

2) Age: 10 years or younger

3) Visual acuity in the amblyopic eye: 0.2 to 0.8 (log MAR 0.1 to 0.7)

4) Visual acuity in the non-amblyopic eye: better than 1.0 (log MAR 0)

5) Eye position: orthophoria, heterophoria, or interemittent hetertropia.

6) Bagolini striated lens test : binocular single vision with peripheral fusion

Exclusion criteria:

1) Eye diseases other than refractive error, amblyopia, and strabismus

2) Systemic or neurological diseases affecting visual function

3) Inability to wear spectacles to correct refractive errors

4) A history of photosensitive epilepsy

Baseline examination

We measured distance and near visual acuity. The power of their spectacles was checked and, if necessary, cycloplegic refraction was performed with 1% cyclopentolate eye drops. We measured the distance and near deviation of the eyes using the alternate cover test with prisms and assessed binocular function using the Bagolini striated lens test and the TNO stereopsis test (R) (TNO). We also assessed the contrast sensitivity using CSV-1000 (R) (Vectorvision, USA). This instrument provides four rows of sine-wave gratings each of which consists of spatial frequencies of 3, 6, 12, and 18 cycles/degree (cpd). In each row, eight pairs of targets (from No.1 to No.8) with/without striped patterns are lined up from top/bottom. Contrast decreases in order, making it difficult to indicate which are the striped patterns. We regarded the correct number as the contrast sensitivity and converted it into log units. We also assessed the depth of suppression in amblyopic eyes with a Bagolini filter bar (Sbisa Ophthalmic Instruments, Firenze, Italy). In practice, the filter number (from No. 0 to No.17) induced a change in fixation or the appearance of binocular diplopia while placing the filter bar in front of the non-amblyopic eye and increasing the transmittance.

Intervention

We determined the transmittance of BF so that the input of visual information to both eyes would be almost the same, that is, transmittance that induced a change in fixation or the appearance of binocular diplopia with a Bagolini striated lens while placing the filter bar in front of the non-amblyopic eye and increasing the transmittance. Then, we attached a filter in front of the non-amblyopic eye to the child's own corrective and polarized training spectacles were worn (described below) from above. We gave each patient a tablet customized for visual function training, Occlupad(R) (Japan Focus Co. Ltd). They were instructed to play computer action games while wearing the training glasses for one hour a day (Fig. 1a & b). The use of BF was limited to during games because it usually made the use of corrective glasses difficult.

Follow-up visits

The patients visited 4, 8, and 12 weeks after starting the treatment to evaluate visual function. Depending on the depth of suppression in the amblyopic eye, we changed the BF transmittance if required at the 4-week visit, and we terminated the treatment at the 8-week visit. At the 12-week visit, we evaluated the visual function again to see whether the efficacy had been maintained; the patients underwent no treatment other than the refractive glasses in this period.

Statistical Analysis

The measured decimal visual acuity was converted to log MAR. The Friedman's test with post-hoc analysis was used to compare visual acuity (SPSS statistics 27, IBM, Armonk, NY, USA). The Spearman's rank correlation coefficient was also used to estimate the strength of the two variables. The one-way ANOVA with post hoc analysis was used to compare contrast sensitivity for each spatial frequency. We regarded a p-value of 0.05 or less as significant.

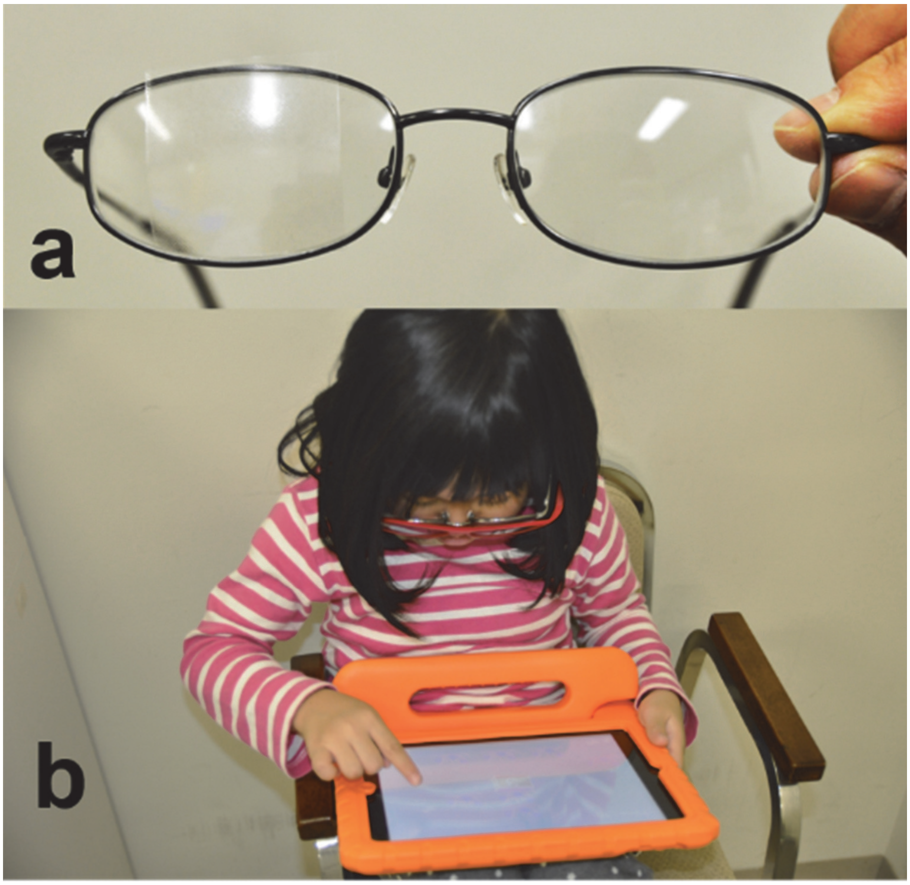

Fig. 1. Bangerter occlusion filter attached to the right lens (a) and treatment setting with a tablet customized for visual function training, Occlupad (R) (b).

Table 1. Summary of diagnosis and clinical characteristics.

patient No.	age(years) / sex	type of amblyopia	Amblyopic eye	history of strabismus surgery	APCT		Bagolini SG		TNO (sec)	suppression depth (No.)
					distance	near	distance	near		
1	7/F	mixed	L	−	25⊿ XT 6-8⊿ RHT	10⊿ XT	L) supp	BSV	−	8
2	8/M	mixed	R	+	4⊿ XT	4⊿ ET	BSV	BSV	−	14
3	9/F	microtropic	R	−	10-12⊿ ET	6⊿ ET	BSV	BSV	−	9
4	9/M	mixed	R	−	ortho	ortho	BSV	BSV	240	11
5	7/F	mixed	R	−	30⊿ XT 8⊿ LHT	30-35 ⊿ XT	L) supp	BSV	−	11
6	8/M	mixed	R	−	ortho	4⊿ ET	BSV	BSV	−	14
7	8/F	mixed	R	−	6⊿ XT	ortho	BSV	BSV	−	11
8	8/M	microtropic	R	−	10⊿ XT	10⊿ XT	BSV (+/-)	BSV (+/-)	−	17

XT: exotropia, ET: esotropia, RHT: right hypetropia, LHT: left hypertropia, supp: suppression. Suppression depth is presented as the number of the Bagolini filer bar (No. 0 to No. 17 from light to dark filters).

RESULTS

Eight patients (four boys) participated in the study (mean ± SD age: 8.0 ± 0.8 years, age range: 7-9 years). The clinical characteristics are summarized in Table 1. In all patients, peripheral fusion was observed at least at near, and gloss near stereopsis was found in patient #4. Patient #2 had a history of strabismus surgery in the amblyopic eye.

Table 2. Distance log MAR at each scheduled visit

patient No.	baseline			4 weeks			8 weeks		12 weeks	
	amblyopic eye	non-amblyopic eye	Bangerter filter No.	amblyopic eye	non-amblyopic eye	Bangerter filter No.	amblyopic eye	non-amblyopic eye	amblyopic eye	non-amblyopic eye
1	0.22	-0.18	0.2	0.12	-0.18	0.2	0.15	-0.18	0.19	-0.16
2	0.19	-0.18	0.2	0.26	-0.18	0.2	0.15	-0.18	0.40	-0.18
3	0.12	0.00	0.2	0.10	0.07	0.2	0.12	0.05	0.22	-0.08
4	0.22	-0.18	0.2	0.19	-0.18	0.2	0.15	-0.30	0.30	-0.16
5	0.40	-0.18	0.2	0.40	-0.08	0.2	0.52	-0.18	0.40	-0.18
6	0.40	-0.18	< 0.1	0.19	-0.18	0.1	0.19	-0.18	0.22	-0.18
7	0.70	-0.18	< 0.1	0.46	-0.18	< 0.1	0.46	-0.18	0.35	-0.18
8	0.30	-0.18	0.4	0.19	-0.18	0.4	0.26	-0.18	0.52	-0.16
mean	0.32	-0.15		0.24	-0.13		0.25	-0.16	0.32	-0.16
SE	0.06	0.02		0.05	0.03		0.05	0.03	0.04	0.01
p-value *	-	-		0.035	n.s.		n.s.	n.s.	n.s.	n.s.

The shaded columns indicate treatment period. * : p-value for the Friedman's test with post-hoc analysis to compare the visual acuity at each scheduled visit.

Effect on distance visual acuity

The mean log MAR of amblyopic eye at distance improved significantly from 0.32 to 0.24 in the first four weeks of treatment (Friedman test with post-hoc analysis, $p < 0.05$, Table 2). This effect seemed to persist (0.25), but was not significant at the 8-week visit. At the 12-week visit (four weeks after terminating the treatment), however, the mean log MAR returned to the baseline level. We found no change in the log MAR in the non-amblyopic eye throughout the follow-up period.

Table 3. Near log MAR at each scheduled visit

patient No.	baseline	4 weeks	8 weeks	12 weeks
1	0.22	0.15	0.12	0.26
2	0.40	0.15	0.10	0.30
3	0.15	0.19	0.12	0.12
4	0.19	0.12	0.19	0.26
5	0.30	0.35	0.46	0.52
6	0.19	0.19	0.26	0.26
7	0.60	0.46	0.22	0.52
8	0.26	0.12	0.10	0.22
mean	0.29	0.22	0.20	0.31
SE	0.05	0.04	0.04	0.05
p-value *	–	n.s.	n.s.	n.s.

The shaded columns indicate treatment period.
* : p-value for the Friedman's test with post-hoc analysis to compare the visual acuity at each scheduled visit.

Effect on near visual acuity

At baseline, the mean log MAR of amblyopic eye at near was 0.29, but there was a trend towards improvement to 0.22 and 0.20 at the 4- and 8-week visits, respectively, but none of these changes was significant (Table 3). At the 12-week visit (four weeks after terminating the treatment), the near visual acuity also tended to return to the baseline level.

Effect on contrast sensitivity

Table 4 shows the log contrast sensitivity of amblyopic eyes at each scheduled visit. Contrast sensitivity significantly improved at a low spatial frequency (3 cpd) at the 4- and 8-week visits (one-way ANOVA with post hoc analysis, $p < 0.05$), and the therapeutic effect persisted until four weeks after terminating the treatment (12-week visit). On the other hand, there was no significant change at 6, 12, or 18 cpd throughout the follow-up period. In non-amblyopic eyes, there was no significant change at any spatial frequency.

Depth of suppression and distant log MAR

Fig. 2 shows the relationship between the depth of suppression for the amblyopic eye at baseline and distance log MAR at each scheduled visit. At the 12-week visit only (Fig. 2d), we found a

Table 4. Log contrast sensitivity at each scheduled visit

spatial frequency (cycle /degree)	baseline		4 weeks		8 weeks		12 weeks	
	amblyopic eye	non-amblyopic eye	amblyopic ye	non-amblyopic eye	amblyopic ye	non-amblyopic eye	amblyopic ye	non-amblyopic eye
3	1.31 ± 0.06	1.71 ± 0.06	1.61 ± 0.06*	1.74 ± 0.04	1.62 ± 0.10*	1.80 ± 0.04	1.65 ± 0.08*	1.76 ± 0.08
6	1.65 ± 0.12	1.99 ± 0.05	1.73 ± 0.07	2.05 ± 0.05	1.71 ± 0.06	2.03 ± 0.08	1.82 ± 0.09	2.01 ± 0.07
12	1.30 ± 0.11	1.66 ± 0.07	1.21 ± 0.16	1.69 ± 0.07	1.16 ± 0.13	1.71 ± 0.06	1.21 ± 0.14	1.62 ± 0.12
18	0.75 ± 0.14	1.23 ± 0.09	0.77 ± 0.12	1.23 ± 0.09	0.60 ± 0.12	1.29 ± 0.07	0.72 ± 0.12	1.27 ± 0.09

*: $p < 0.05$ with the Friedman's test with post-hoc analysis to compare the contrast sensitivity at each scheduled visit. The shaded columns indicate treatment period.

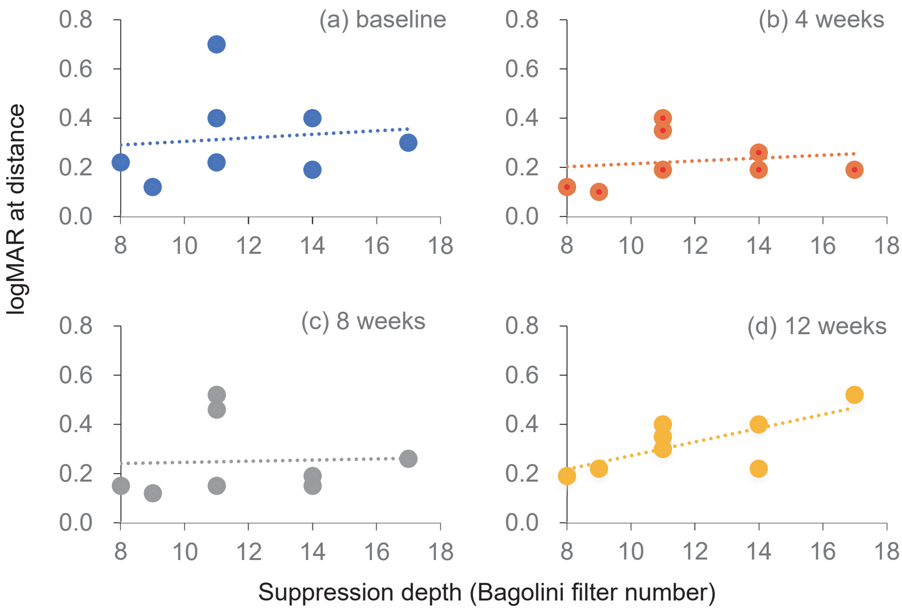

Fig. 2. The relationship between suppression depth at baseline and log MAR at distance.
The dashed lines show least-squares regression lines. The correlation between the suppression depth and log MAR was significant only at the 12-week visit: $y = 0.0278x - 0.0056$, $r = 0.71$, $p = 0.049$.

significant correlation between them (Spearman's rank correlation coefficient, $r = 0.71$, $p < 0.05$).

DISCUSSION

Our binocular treatment using BF and computer games significantly improved distance visual acuity in patients with intractable unilateral amblyopia, although the treatment was only for one hour a day. As reported by Pediatric Eye Disease Investigator Group[6], it may be possible to expect a treatment effect similar to that of occlusion therapy in cases of poor adherence to conventional treatments. As in previous reports, we found no adverse effect on the visual function of the non-amblyopic eye[10]. However, four weeks after terminating the treatment, the distance visual acuity returned to the baseline level. This indicates the particular difficulty in maintaining the treatment effect in these patients. In addition, there was no significant treatment effect on near visual acuity, suggesting that, as with distance visual acuity, the amblyopia was still intrinsic even with binocular treatment.

Reportedly, there was no significant correlation between log MAR acuity and depth of suppression in patients with anisometropic amblyopia (mean age 9.7 years), and the suppression of the amblyopic eye was deeper in anisometropic patients with microstrabismus[11, 12]. We examined this relationship in our patients, and did not find a significant relationship between distant visual acuity at baseline and depth of suppression either. On the other hand, there was a significant correlation ($p < 0.05$) with distance log MAR at the 12-week visit (four weeks after terminating the treatment) : patients who had deep suppression of the amblyopic eye at baseline had a poor therapeutic effect after the treatment. If we look at it the other way around, patients who have weak suppression may gain some benefit from this treatment[13].

The contrast sensitivity at 3 cpd was significantly improved by this treatment. In amblyopic eyes, contrast sensitivity at intermediate to high spatial frequencies is usually reduced[14]. In addition, it has been reported that binocular treatment with a BF improved the spatial sensitivity of amblyopic eyes at 3 cpd, but not at 9 cpd[8]. It seems that the therapeutic effect of binocular treatment may be related to the spatial frequency. The lack of improvement at intermediate to high special frequencies, including visual acuity, may be due to the immaturity of lateral suppression. Notably, the improvement at 3 cpd was maintained after the treatment, suggesting that the benefit from amblyopia treatment is not limited to improving visual acuity.

Our study has several limitations. First, we had no control since patients in this age group were at the limit of visual acuity development, it was ethically difficult to set up untreated controls. In addition, the number of patients was small. Also, the use of BF was limited to one hour per day. Finally, the treatment period and the follow-up period were relatively short.

In conclusion, our binocular treatment using a BF and computer games appeared to improve visual function only in terms of contrast sensitivity at a low spatial frequency in patients with intractable unilateral amblyopia. Patients who have weak suppression may gain some benefit from this treatment.

ACKNOWLEGEMENT

This study was supported by a Grant-in-Aid for Scientific Research from the Japanese Ministry of Education, Culture, Sports, Science and Technology (No. 26462656).

CONFLICT OF INTEREST

The following authors have no financial disclosures to report: Takashi Furuse, Kayoko Hasebe, Toshihiro Imai, Yuka Nagata, Sachina Nagao, Tomoki Tokutake, and Satoshi Hasebe.

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