

Treating Amblyopia with Liquid Crystal Glasses: A Pilot Study

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PURPOSE. To evaluate the use of liquid crystal glasses (LCG) for the treatment of amblyopia caused by refractive errors, strabismus, or both.

METHODS. In this noncomparative, prospective, interventional case series, 28 children (age range, 4–7.8 years) with monocular amblyopia participated, of which 24 completed the study. In the LCG, the occluding and nonoccluding phases of the flicker were electronically set in all patients at a fixed rate. The rate was set so that accumulated occlusion was 5 hours during 8 hours' wear time. Occlusion was applied only to the good eye. All 24 children were followed up regularly for 9 months. Best corrected VA for distance and near, fixation patterns, and binocular function were measured. VA for distance was measured with the Snellen chart and for near with the Rossano/Weiss chart.

RESULTS. Mean VA for distance at the end of the study (after 9 months) was 0.59 (SD, 0.16) compared with 0.27 (SD, 0.09) at the beginning ($P < 0.001$). Most of the children (92%) complied well with the treatment. (Good compliance was defined as wearing the LCG for at least 8 hours per day.) Stereopsis at the end of treatment was good (better than 60 sec arc) in 21% of the children compared with 8% at the beginning. No serious adverse events were recorded.

CONCLUSIONS. The use of LCG in patients with amblyopia yielded an improvement in near and distance VA and in stereopsis. Treatment was well accepted by children and parents. (*Invest Ophthalmol Vis Sci.* 2010;51:3395–3398) DOI:10.1167/iov.09-4568

Clinical and experimental observations have led to the conclusion that an active central nervous system mechanism is responsible for the development of amblyopia. Visual inputs

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to the cortex are regulated and processed under the control of the dominant eye, which actively suppresses potential inputs from the amblyopic eye.¹ Accordingly, for nearly three centuries, the mainstay of treatment for amblyopia has been occlusion of the sound eye. The time advocated for daily patching of the sound eye may vary from a few hours to all of the child's waking hours,^{2,3} and treatment success rates also vary markedly.⁴ The wide variation is probably influenced by numerous factors, both known and unknown. Among the known factors that strongly influence visual improvement are poor compliance on the part of parents and the child's unwillingness to occlude the sound eye, the latter factor being especially common at 3 to 7 years of age. It has been suggested that the difficulty in assuring treatment compliance has been overcome by electronic monitoring of patching.^{5,6}

Since patching and atropine treatments are not universally successful and are resisted by some children and parents, there is a need for alternative treatment modalities. As a potential alternative for amblyopia treatment, electronically engineered liquid crystal glasses (LCG) have been devised. The safety and feasibility of this new approach has been reported by our group.⁷ We extend our previous observations and describe the results of a multicenter pilot study in which this new technology was tested.

MATERIALS AND METHODS

Liquid Crystal Glasses

The use of LCG, in which an electronic shutter controlled by a pre-programmed microchip is incorporated into the optical refractive lens, represents a new approach to the treatment of amblyopia. The thin glass liquid crystal shutter is applied to the strong eye and is coupled to the refractive lens. The liquid crystal shutter comprises large organic molecules that manifest an electric polarity and are suspended in a gel-like liquid between two thin glass plates coated with thin polarizer film. When an electric voltage is applied to this shutter, the spatial orientation of the suspended molecules is changed and the polarity of the light is rotated. The rotated light is thus blocked by the outer polarizing film and creates a "black" lens. This action, allows the shutter to alternate between clarity (OFF/OPEN), when no voltage is applied, to a black, highly opaque state, and ON/CLOSED, when voltage is applied.⁶ (The liquid crystal shutter meets U.S. Food and Drug Administration [FDA] safety standards.)

Because of the characteristics of the polarizer film, in the clear state, the lens with the coupled shutter has a slightly greenish color. For balanced viewing, the amblyopic eye lens is slightly tinted, so as to resemble more closely the appearance of the lens with the liquid crystal shutter.

The occlusion process is electronically controlled by a device that comprises a microprocessor with a memory and is powered by rechargeable coin batteries. The rate and duration of each viewing state are preprogrammed at a defined, controlled pace. In clinical practice, the flickering rate can be preprogrammed for individual patients by the

physician. In this study, the glasses were preprogrammed by the manufacturer to provide occlusion 66% of the time, an equivalent of 5 hours of occlusion during 8 hours of glasses wear. On average, the ON (occlusion) time was ~40 seconds and the OFF state (open) was ~20 seconds of each minute.

To enable the child to adjust more easily to the flickering, the LCG was preprogrammed to start at a low occlusion rate, increasing gradually over 10 days to the steady state rate. The lenses for both the sound eye and the amblyopic eye carried the prescribed refractive correction, if any, for each child. The liquid crystal shutter was applied only to the good eye.

The glasses were activated by the child (or parent), by gently pressing a microswitch on donning the glasses. Deactivation was obtained by another press when the glasses were not in use.

On activation of the LCG the active time was recorded in the memory of the electronic controller. The information was displayed on a reporting box that also served as a charger of the glasses' batteries when the glasses were plugged in overnight. The information on the wear time was retrieved from the glasses and displayed digitally, and a smiley or sad-faced icon indicated compliance or noncompliance. (Because of technical problems with this feature that occurred during the study, the parents were asked to report subjectively on compliance level. Good compliance was reported if the child had worn the LCG for at least 8 hours per day.)

The comparison was made between the patient's initial prestudy visual performance of the amblyopic eye and the performance at the end of the study.

The detailed protocol for this study was reviewed and approved by the Ethics Committees of the three participating medical centers (Ministry of Health, Approval Grant HT 2439) and complied with the Declaration of Helsinki.

The purpose of the study was not to compare the LCG method with other treatment methods such as patching, but rather to investigate the effectiveness and safety of the glasses in treating moderate amblyopia in children under 8 years of age.

Patients

Twenty-eight children with monocular amblyopia due to anisometropia, strabismus, or both were enrolled in the study. The children were outpatients at the pediatric ophthalmology units of three medical centers in Israel (Sheba Medical Center, Tel Hashomer; Sapir Medical Center, Kfar Saba, and Hadassah Hebrew University Hospital, Jerusalem). Excluded from the study were candidates who had undergone intraocular surgery or who had high myopia (>6D), ocular disease as the cause of the reduced visual acuity (VA), strabismus due to extraocular muscle fibrosis, or a family or personal history of epilepsy. Four of the enrolled children were excluded from the study because they either failed to present themselves for regular follow-up or stopped using their LCG glasses prematurely. (One child did not appear at the first visit, one child stopped after two follow-up visits, and two withdrew after four follow-up visits.) The rest, all of whom used the LCG constantly and attended the scheduled clinic visits on a regular basis over the planned study period of 9 months, comprised the study group. In these 24 children, amblyopia was due to anisometropia in 7, strabismus in 6, and both anisometropia and strabismus in 11. All met the additional inclusion criteria of compliance; and VA of 20/120 to 20/40 in the amblyopic eye and at least 20/40 in the sound eye, with at least three lines of difference between the two eyes; no prior treatment for amblyopia during the previous month; and any refractive errors corrected for at least the previous 4 weeks. It should be noted that there was only one case in which the child had been wearing glasses for 4 weeks, and all the rest of the anisotropic children had worn the glasses for more than several months before the study. Three children had no refractive error and therefore were prescribed 0-D lenses.

Study Protocol

During enrollment (visit 0) and at each of the six scheduled visits, each patient underwent a thorough eye examination. VA for distance (Snellen chart) and for near (Rossano/Weiss chart) in the sound eye and in the amblyopic eye were assessed while the patient was wearing their prescribed glasses, if any. Scoring of Snellen VA (letters or pictures presented in lines) was according to standard logMAR letters; for example, 20/20 was defined as 1.0, 20/25 as 0.8, and so on. Strabismus was measured for near and distance by the alternate prism cover test. Binocular functions were assessed in cooperative children by using the fly, animals, and circles parts of the Titmus stereopsis test. Slit lamp examination and funduscopy were performed in all patients. Full cycloplegic refraction was performed 40 minutes after tropicamide 0.5% (Mydramide; Fischer Pharmaceutical Labs. Ltd., Tel-Aviv, Israel) and cyclopentolate 1.0% eye drops had been instilled twice with a 15-minute interval between instillations.

Follow-up

After the baseline visual performances with the LCG had been assessed (visit 1), the parents were briefed about handling and care of the LCG and the need to charge the electronic control batteries overnight. They were also asked to record any unusual events that occurred during the study period and to verify that the electronic shutter was functioning properly when the child started wearing the glasses each morning. They were also taught how to initiate the mechanism manually in case of electronic failure of the shutter's flicker function and were instructed to inform us of the problem. Each child received two pairs of glasses to ensure continued use in case of a technical problem.

A follow-up visit was scheduled every 5 to 6 weeks during the 9-month period of the study (visits 2-6). After the sixth follow-up visit, wearing of the LCG was discontinued, and corrective regular glasses were prescribed as needed.

During each visit, the parents were asked to subjectively evaluate any technical problems encountered with the LCG, their child's willingness to wear them, and the length of time for which they were worn.

Assessments of visual performance, similar to those performed during visits 0 and 1, were performed in a semimasked fashion. The examiners knew that the patient was participating in the study but did not have clinical information and did not know what each patient's previous visual performance was.

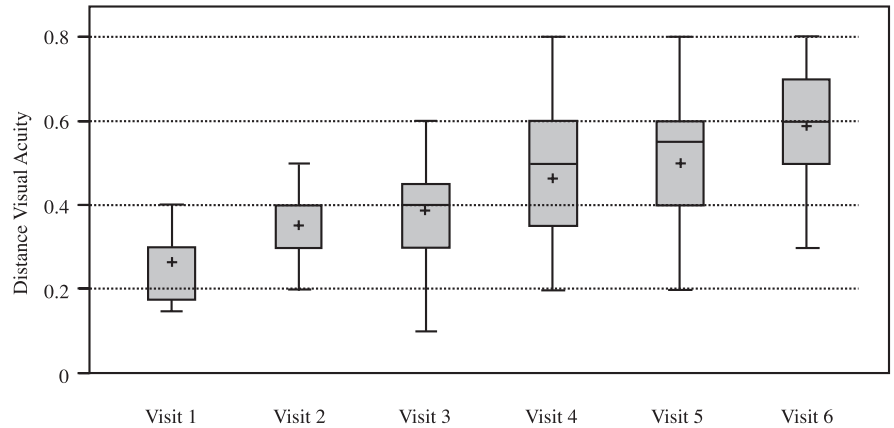
Data Analysis

The trial data were captured on a computerized CRF (case report form), developed specifically for this study. All subjects who were enrolled in the study and had valid data were included in the analyses (SAS ver. 9.1; SAS Institute, Cary NC). Study data are presented in the form of graphs and tables. Continuous variables are presented as the mean and SD or with a 95% confidence interval. Count data are summarized by a percentage with 95% exact binomial confidence limits where relevant. The statistical significance of the change from baseline VA at each visit was assessed with a Wilcoxon signed ranks test. $P < 0.05$ or less was considered statistically significant.

RESULTS

Characteristics of the Study Population

Of the 24 children included in the study, 8 were girls and 16 were boys. The age range was 4.0 to 7.8 years, with a mean age of 6.1 (SD, 1.2) years. Amblyopia was present in the right eye in 10 children and in the left eye in 14. Before entering the study, 11 patients had undergone treatment attempts by patching or atropine eye drops, but vision failed to improve in the amblyopic eye. Of those, nine had poor compliance, and two had high compliance but no improvement in vision. Previous offers of treatment by occlusion therapy had been refused by



Descriptive Statistics	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6
Mean	0.27	0.35	0.39	0.46	0.54	0.59
Std Dev	0.09	0.13	0.14	0.15	0.17	0.16
25th Percentile	0.18	0.30	0.30	0.35	0.40	0.50
Median	0.30	0.30	0.40	0.50	0.55	0.60
75th Percentile	0.30	0.40	0.45	0.60	0.60	0.70

FIGURE 1. Distance VA of the amblyopic eye at the beginning of the study (visit 1) and during the study.

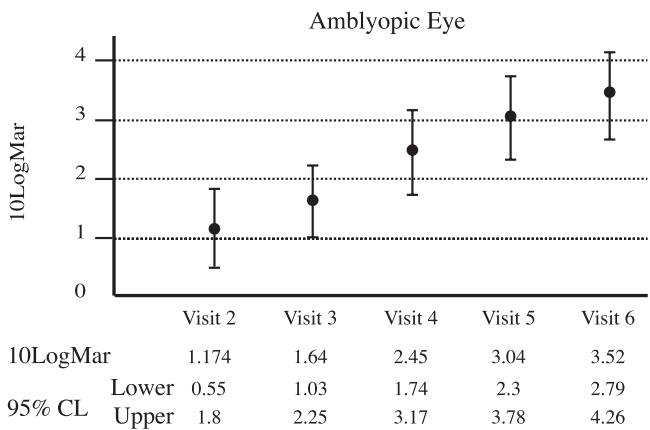
13 children. The cause of amblyopia was nonalternating esotropia in 6 (25%) children, uncorrected refractive error in 7 (29.2%), and strabismus combined with refractive error in 11 (45.8%).

Visual Performance of the Amblyopic Eye

Figure 1 shows the best corrected VA for distance recorded during the six visits. Mean VA was 0.27 (SD, 0.09) at visit 1 and 0.59 (SD, 0.16) at visit 6.

The steady and consistent improvement of VA during each consecutive visit relative to visit 1 was significant ($P < 0.001$ for each visit). Figure 2 illustrates these performances on a 10-logMar scale.

As shown in Table 1, by visit 6, 79% of the treated children had improved by 3 lines or more or had achieved a VA of 20/30. Notably, 20% had achieved this level of visual performance after the first visit. Improvement in the VA for distance was accompanied by a significant improvement in near vision (reading). More than 80% of the treated patients showed improvement in near VA to 0.4 (normal vision with the Rossano/Weiss chart is 0.5) or better when examined during visit 6.



* $P < 0.001$ > for comparison of all visits to visit 1

FIGURE 2. Progress of change from baseline VA, measured as 10 logMAR lines.

Binocular Vision

Most of the children in the study had no stereopsis or only gross stereopsis. By the end of the study (visit 6), however, 21% demonstrated good stereopsis (better than 60 sec arc) compared with only 8% at the start of the study.

Visual Functions of the Sound Eye

Distance and near visual acuities of the sound eye remained unchanged throughout the study (data not shown).

Compliance

Of 24 children, 22 (92%) wore the glasses at least 8 hours per day, as requested.

Safety

No serious adverse events were recorded.

The children adjusted to the flickering of the lens of the strong eye easily. Four children had transient headaches, and four events of discomfort were reported. These did not cause them to stop using the LCG. There was no regression (reverse amblyopia) in the VA of the sound eye.

TABLE 1. VA Outcomes

Outcome	Visit					
	1	2	3	4	5	6
Improved Distance VA, %*	—	21	33	46	54	79
95% Confidence limits						
Lower	—	13	16	26	33	58
Upper	—	42	55	67	74	93
Near VA (%)†	38	54	62	79	88	88
95% Confidence limits						
Lower	19	33	41	58	68	68
Upper	59	74	81	93	97	97

* Improved distance visual acuity of 3 lines or more or visual acuity of 0.66 (20/30).

† Near visual acuity of 0.4 or more (Rossano-Weiss chart).

DISCUSSION

The results of this study demonstrate an average improvement in VA of 3.5 logMAR lines over 9 months of use of glasses fabricated with liquid crystal technology that provide an electronically controlled intermittent occlusion of the sound eye, thereby allowing for visual stimuli input to the amblyopic fellow eye. The results also demonstrated that the LCG are safe and have no side effects.

Despite individual variations in the amount of improvement in the tested parameters, at least some improvement in the visual performances of the amblyopic eye was recorded in all treated children. During the first 2 to 3 weeks of the treatment, most of the children were aware of the flickering shutter and the obstruction of visual inputs from the sound eye when the ON stimulus was triggered. However, this awareness decreased over time, and the flickering was hardly noticed. Also of interest is the improvement in binocular visual function observed in some of the children, possibly because the rapid rate of flickering allowed binocular spatial clues to be perceived. The study size of 24 children treated in three different centers did not permit personal tailoring of the treatment period or the flickering rate. It is possible that the success rate for all the tested parameters would be higher if treatment with LCG were individually customized and adapted. This possibility will be examined in a study with a larger number of children, to be performed in the near future.

In the present study, we confirm our previous observations with regard to the safety of the LCG.⁷ We also show that amblyopia caused by refractive error, strabismus, or a combination of both can be treated by LCG. Patient compliance with LCG wear in our study was very good. The early withdrawal of four enrolled children occurred for various personal reasons, but all the rest completed the study. Peak improvement in distance VA was achieved very rapidly in 20% of the treated children, whereas in most of the group, the maximum improvement was reached only after a longer period. These observations are in line with those reported in studies where the treatment modality was patching.⁴ We also found that relative to VA for distance, improvement in reading (near task) acuity was achieved earlier and reached its maximum level earlier. An interesting finding was the significant improvement in stereopsis recorded in 21% of the children. This improvement could have occurred because the use of LCG allows for visual function stimuli of the amblyopic eye while both eyes

remain open, enabling binocular interactions to develop. However, one cannot exclude that improved VA in the amblyopic eye resulted in better stereo acuity.

In summary, we demonstrated that LCG is an effective new device for amblyopia treatment. Bearing in mind the need for extended periods of treatment in some types of amblyopia, we are looking into the possibility of programming the pattern of the LCG flickering sequence on an individual basis for those children who need it. We believe that the potential benefit of the treatment could be substantially enhanced if the flickering sequence were adapted to suit the depth of amblyopia, the required duration of treatment, and the age of the patient. Varying the flickering sequence during the treatment period according to the visual function behavior of the amblyopic eye may enhance the LCG's efficiency.

Many of the amblyopic children wear glasses to correct ametropia. In our study, the glasses were used also for occlusion without the need for additional patch or use of eye drops.

The advantages of the LCG treatment modality demonstrated in the present study could also be further improved by inserting specifically designed electronic processors into the shafts of the glasses. These devices could be programmed to deliver a personally adapted flickering rate, which could also be modulated according to clinical experience and the performance of the amblyopic eye.

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