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An eye-tracking-based dichoptic home treatment for amblyopia: a multicenter randomized clinical trial

Luisa M. Hopker[1], Júlia D. Rossetto[2]

1. Hospital de Olhos do Paraná, Curitiba, PR, Brazil.
2. Departamento de Oftalmologia, Universidade Federal do Rio de Janeiro, Rio de Janeiro, RJ, Brazil.

Importance: The study by Wygnanski-Jaffe et al. is the first study to prove that dichoptic treatment is neither inferior nor superior to patching for the treatment of amblyopia.

CureSight (NovaSight, Ltd) is a new digital dichoptic device for home binocular treatment that is based on watching video content. A visual stimuli is streamed on a monitor via two separate digital channels, one for each eye. The system blurs the central vision of the nonamblyopic (fellow) eye using real-time gaze tracking. The blurred area and its intensity are adjusted automatically according to the visual acuity (VA) of each eye as registered by the physician on the CureSight cloud during the follow-up visits. Furthermore, a monitoring center tracks patients' adherence remotely.

Study design: The randomized clinical trial (RCT) was registered at clinicaltrials.gov (No: NCT04785690). This prospective, multicenter, randomized (1:1), masked and controlled study compared the visual outcomes of an eye tracking-based dichoptic home treatment with those of the standard amblyopia treatment (patching). CureSight is an amblyopia treatment manufactured by NovaSight, Israel. Currently, CureSight is FDA-approved and complies with the guidelines of the EU Medical Device Regulation.

Children aged 4-9 years who were diagnosed with amblyopia and small-angle strabismus, anisometropia, or both were included in the study. All the patients had an interocular difference of two lines or more and a best-corrected VA (BCVA) of 20/32 to 20/100 in the amblyopic eye (mild-to-moderate amblyopia). The BCVA of the fellow eye was 20/40 or better among patients aged 4-5 years and 20/32 or better among patients aged 5-7 years. Strabismus was limited to tropia up to 5 prism diopters (PD) or heterophoria up to 10 PD. The children were required to have a stable VA with their best refractive correction before enrollment. Both previously treated and untreated patients were included in the study.

Patients in the binocular treatment group were prescribed the CureSight home treatment for 90 minutes per day, 5 days per week, for a total of 16 weeks (total of 120 hours). Patients in the control group (patching) were prescribed a patch for the nonamblyopic eye that had to be worn for 2 hours per day, 7 days per week, for a total of 16 weeks (total of 224 hours).

The primary outcome of the study was the mean improvement in VA in the amblyopic eye from the baseline. The secondary and additional outcomes were the change from baseline in the stereoacuity test score, amblyopic eye near VA, binocular VA, and binocular near VA. Safety of the intervention was evaluated on the basis of the frequency, severity, and causality of adverse events (AEs).

Results: A total of 103 children with amblyopia were randomized into the binocular treatment (n=51) and patching (n=52) groups. The 16-week outcome data of 95 participants were available and included in the primary analysis. Approximately 51% of the participants had not been previously treated with a patch or atropine penalization. A majority of the children had anisometropic amblyopia (92%).

A VA improvement of 0.28 ± 0.13 logMAR and 0.23 ± 0.14 logMAR was observed in the binocular treatment and patching groups, respectively ($p<0.0001$ for both). Thus, binocular treatment was not inferior to patching in improving the amblyopic eye VA.

Corresponding author: Luisa M. Hopker.
E-mail: luhopker@gmail.com

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The stereoacuity (0.40 vs. 0.40 log arcseconds) and binocular VA (0.13 logMAR vs. 0.09 logMAR) had improved from the baseline in the binocular treatment ($p<0.0001$ for both) and patching ($p<0.0001$ for both) groups. However, these improvements in stereoacuity (difference, 0; 95% CI, -0.27 to -0.27; $p=0.76$) and binocular VA (difference, 0.041; 95% CI, -0.002 to 0.085; $p=0.07$) were not significantly different between the two groups. Furthermore, a significantly higher adherence was observed in the binocular treatment group than in the patching group (91% vs. 83%; 95% CI, -4.0 to 21; $p=0.011$). No serious AEs or unanticipated AEs developed in the study.

Limitations: The absence of treatment groups which included strabismic and privation amblyopia was a limitation of the study. Another limitation of the study was the lack of different dose-response protocols, including nondaily regimens for in-office treatments, to evaluate the impact of dosing on the rapidity of visual improvement. Furthermore, the current study protocol of treating patients for 6 days a week at their homes could impede its applicability in other countries.

The lack of follow-up after treatment cessation to access treatment durability and the need for a weaning treatment strategy are other limitations of this study. Furthermore, the use of a subjective self-logging compliance diary by the guardians of the patients in the patching group may have overestimated the compliance.

Clinical relevance: This study is a crucial turning point in this field of study. It is the first RCT to compare a novel treatment for amblyopia with the old-fashioned and effective patching approach and demonstrate similar outcomes. Although amblyopia is a common disease, studies involving its treatment often have serious methodological flaws. Although dichoptic treatments have been explored in the past[1-6], most studies have had a short follow-up period and/or no comparison with a patching group[1-6].

This study by Wygnanski-Jaffe et al. was a well-designed RCT, which included patients with almost exclusively anisometropic amblyopia. Furthermore, patients with strabismus who only had a minimal angle of deviation or mild compensated deviation were included. Before being enrolled in the study, the patients were required to exhibit a stable VA after refraction correction. This ensured that improvements with treatment were not falsely and solely attributed to adequate correction.

The study compared a novel device with the gold standard approach (patching) that were administered over 16 weeks, which is appropriate for amblyopia treatment. The VA improvement in both age groups (4-7 and 7-9 years) may encourage amblyopia treatment beyond the usual age of treatment (up to 7 years).

The study results demonstrate that dichoptic treatment can be considered an alternative to occlusion in the treatment of amblyopia, with the same effectiveness and significantly greater adherence. Because the treatment offers children unlimited streamed visual content with continued support from a monitoring center, the treatment adherence will likely remain high even outside the rigor of a clinical study. However, the proposed treatment demands the need of a device which is costlier than a patch. Nonetheless, binocular treatment may be a better accepted and nonstigmatizing alternative to the patch in affluent populations.

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