Randomized Trial to Evaluate Combined Patching and Atropine for Residual Amblyopia

Many children fail to achieve normal visual acuity after treatment for amblyopia.1,2 This remaining deficit may be called residual amblyopia. We conducted a randomized trial to determine whether an intensive final push with combined patching and atropine sulfate can improve visual acuity in children with residual amblyopia.

Methods. A parent or guardian of each study subject gave written informed consent. The protocol is available at http://www педig.net. Eligible subjects were aged 3 to younger than 10 years and had strabismic and/or anisometropic amblyopia, best-corrected visual acuity of 20/32 to 20/63 in the amblyopic eye, interocular visual acuity difference of 2 or more lines, and no improvement in visual acuity in the amblyopic eye between 2 consecutive visits at least 6 weeks apart while patching 6 hours per day or using daily atropine. Spectacles, if prescribed (based on investigator discretion), met the criteria in eTable 1 (http://www.archophthalmol.com). All subjects wore spectacles except those with purely strabismic amblyopia. Additional eligibility criteria are listed in eTable 1. Subjects were randomized with equal probability to the following: (1) treatment with 6 hours of prescribed patching combined with daily atropine (intensive group); or (2) a reduction of current treatment for 4 weeks with 2 hours of prescribed daily patching or once-weekly atropine followed by spectacles alone if needed (weaning group). Randomization was accomplished using a permuted-blocks design stratified by site and by current treatment with patching or atropine. The primary outcome was masked assessment of visual acuity by isolated crowded Amblyopia Treatment Study HOTV (for subjects aged 3 to <7 years)1 or Electronic Early Treatment Diabetic Retinopathy Study (for subjects aged 7 to <10 years)4 optotypes at 10 weeks. Subjects with improvement of 2 or more lines from logistic regression controlling for baseline visual acuity. One subject missing the primary outcome examination in the weaning group was considered to have not improved 2 or more lines for analyses.

Results. Between October 1, 2007, and March 30, 2009, 27 subjects were randomized to the intensive group and 28 were randomized to the weaning group. The average age was 6.9 years; 23 subjects (85%) were female, and 40 subjects (73%) were white. At the time of enrollment, 39 subjects (71%) were being treated with patching and 16 (29%) were being treated with daily atropine. The 2 groups appeared balanced with respect to baseline characteristics (eTable 2), except that those in the intensive treatment group were more likely than those in the weaning group to have a difference in visual acuity of more than 8 lines at baseline and those in the weaning group were more likely than those in the intensive treatment group to have both a difference in visual acuity of more than 8 lines at baseline and improvement of 2 or more lines from logistic regression controlling for baseline visual acuity. One subject missing the primary outcome examination in the weaning group was considered to have not improved 2 or more lines for analyses.

Abbreviation: CI, confidence interval.

aVisual acuity testers were masked for the primary outcome examination. 

Results. Between October 1, 2007, and March 30, 2009, 27 subjects were randomized to the intensive group and 28 were randomized to the weaning group. The average age was 6.9 years; 23 subjects (85%) were female, and 40 subjects (73%) were white. At the time of enrollment, 39 subjects (71%) were being treated with patching and 16 (29%) were being treated with daily atropine. The 2 groups appeared balanced with respect to baseline characteristics (eTable 2), except that those in the intensive treatment group were more likely than those in the weaning group to have a difference in visual acuity of more than 8 lines at baseline and those in the weaning group were more likely than those in the intensive treatment group to have both a difference in visual acuity of more than 8 lines at baseline and improvement of 2 or more lines from logistic regression controlling for baseline visual acuity. One subject missing the primary outcome examination in the weaning group was considered to have not improved 2 or more lines for analyses.

Abbreviation: CI, confidence interval.

aVisual acuity testers were masked for the primary outcome examination. 

Results. Between October 1, 2007, and March 30, 2009, 27 subjects were randomized to the intensive group and 28 were randomized to the weaning group. The average age was 6.9 years; 23 subjects (85%) were female, and 40 subjects (73%) were white. At the time of enrollment, 39 subjects (71%) were being treated with patching and 16 (29%) were being treated with daily atropine. The 2 groups appeared balanced with respect to baseline characteristics (eTable 2), except that those in the intensive treatment group were more likely than those in the weaning group to have a difference in visual acuity of more than 8 lines at baseline and those in the weaning group were more likely than those in the intensive treatment group to have both a difference in visual acuity of more than 8 lines at baseline and improvement of 2 or more lines from logistic regression controlling for baseline visual acuity. One subject missing the primary outcome examination in the weaning group was considered to have not improved 2 or more lines for analyses.

Abbreviation: CI, confidence interval.

aVisual acuity testers were masked for the primary outcome examination. 

Results. Between October 1, 2007, and March 30, 2009, 27 subjects were randomized to the intensive group and 28 were randomized to the weaning group. The average age was 6.9 years; 23 subjects (85%) were female, and 40 subjects (73%) were white. At the time of enrollment, 39 subjects (71%) were being treated with patching and 16 (29%) were being treated with daily atropine. The 2 groups appeared balanced with respect to baseline characteristics (eTable 2), except that those in the intensive treatment group were more likely than those in the
weaning group to have anisometropia or combined mechanism as the cause of amblyopia (17 subjects [63%] vs 12 subjects [43%], respectively) and had more hyperopia in the amblyopic eye (mean spherical equivalent, 5.39 vs 4.24 diopters, respectively).

At the 10-week primary outcome examination, visual acuity in the amblyopic eye improved 2 or more lines from enrollment in 3 of the 27 subjects (11%) in the intensive treatment group and 6 of the 27 subjects (22%) in the weaning group (difference in proportions = −10%; 95% confidence interval).

Weaning group to have anisometropia or combined mechanism as the cause of amblyopia (17 subjects [63%] vs 12 subjects [43%], respectively) and had more hyperopia in the amblyopic eye (mean spherical equivalent, 5.39 vs 4.24 diopters, respectively).
Comment. For children with amblyopia who have already stopped improving with 6 hours of prescribed daily patching or with daily atropine, we found that an intensive final push of combined treatment with patching and atropine did not produce a better visual acuity outcome after 10 weeks compared with a control group in whom treatment was gradually discontinued. Despite our small sample size, it is unlikely that a meaningful effect was missed, since both the upper and lower limits of the 95% confidence interval for the mean difference between treatment groups were less than 1 line.

This study evaluated a select group of children with mild residual amblyopia (visual acuity of 20/32-20/63 inclusive) who had a substantial amount of previous amblyopia treatment. Our results should not be generalized to children with more severe residual amblyopia or those who have stopped improving after less intense treatment.

Pediatric Eye Disease Investigator Group (PEDIG) Writing Committee

Authors/Group Information: The members of the Writing Committee and the Pediatric Eye Disease Investigator Group (PEDIG) participating in the study are listed on page 961.

Correspondence: David K. Wallace, MD, MPH, c/o Jaeb Center for Health Research, 15310 Amberly Dr, Ste 350, Tampa, FL 33647 (pedig@jaeb.org).

Author Contributions: The authors had full access to all of the data in the study, and Dr Wallace takes responsibility for the integrity of the data and the accuracy of the data analysis.

Financial Disclosure: None reported.

Funding/Support: This study was supported by grant EY011751 from the National Eye Institute, National Institutes of Health, US Department of Health and Human Services.

Role of the Sponsor: The funding organization had no role in the design or conduct of the study.

Trial Registration: clinicaltrials.gov Identifier: NCT00506675

Previous Presentation: This paper was presented at the 36th Annual Meeting of the American Association for Pediatric Ophthalmology and Strabismus; April 17, 2010; Orlando, Florida.


COMMENTS AND OPINIONS

Acupuncture and Amblyopia

Zha and colleagues’ description of acupuncture as a new method for treating amblyopia adds to prior studies of diverse therapies. They include, among others, an abundance of occlusion protocols ranging from a few hours per day to complete eyelid suturing, neuroadaptation, periauricular acupuncture, vision training, levodopa-carbidopa, colored lenses, Bangerter filters, supervised near work, playing computer games, perceptual learning, and neurologic organization training. These studies, in common with this latest addition, are characterized by (1) acuity outcomes that are similar to patching therapy and (2) a lack of untreated controls. Most of these are regarded by the American Academy of Ophthalmology Committee on Children with Disabilities as poorly controlled studies that rely on anecdotal information. “Their reported benefits can be explained by the traditional educational remedial techniques with which they are usually combined.”

Supporting this view is a Pediatric Eye Disease Investigator Group’s finding that the acuity of both the amblyopic and fellow eyes substantially improved with increasing age prior to treatment (Table 3).

The influence of placebo or Hawthorne effects (the positive effect on behavior that sometimes occurs in a study or experiment as a result of the interest shown by the experimenter in humans who are being treated, studied, or observed) in these studies has not been seriously considered.

In evaluating this and related articles, it is important to consider the admonition that “A disease which has no treatment has many treatments advocated: it becomes a graveyard of promising and then discarded therapies, some of them even harmful.”

Philip Lempert, MD

Author Affiliation: Cayuga Medical Center, Ithaca, New York.

Correspondence: Dr Lempert, 100 Uptown Rd, Ithaca, NY 14850 (eyechartplus@aol.com).

Financial Disclosure: None reported.