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Randomized Trial to Evaluate Combined Patching and Atropine for Residual Amblyopia

Pediatric Eye Disease Investigator Group*

To the Editor

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 can improve visual acuity in children with residual amblyopia.

Methods

A parent or guardian of each study subject gave written informed consent. The study is listed on www.clinicaltrials.gov (NCT00506675), and the protocol is available at www.pedig.net. Eligible subjects were aged 3 to < 10 years old, with strabismic and/or anisometropic amblyopia, best-corrected amblyopic eye acuity of 20/32 to 20/63, interocular acuity difference ≥ 2 lines, and no improvement in amblyopic eye acuity 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. All subjects wore spectacles except 4 with purely strabismic amblyopia. Additional eligibility criteria are listed in eTable 1. Subjects were randomized with equal probability to (1) treatment with 6 hours of prescribed daily 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)³ or Electronic Early Treatment Diabetic Retinopathy Study[®] (for subjects aged 7 to <10 years) optotypes⁴ at 10 weeks. Subjects in the intensive treatment group discontinued atropine 2 weeks before this examination.

The planned sample size was 240. After a recruitment period of 18 months, 55 subjects had been randomized at 18 sites. The study was stopped, on recommendation of the Data and Safety Monitoring Committee, because of slow recruitment and a conditional power analysis indicating the study was unlikely to find a statistically significant benefit of intensive treatment if the study continued.

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Results

Between October 2007 and March 2009, 27 subjects were randomized to the intensive group and 28 randomized to the weaning group. The average age was 6.9 years; 45% were female; 73% were white. At the time of enrollment, 39 (71%) were being treated with patching and 16 (29%) with daily atropine. The two groups appeared balanced with respect to baseline characteristics (eTable 2), except those in the intensive group were more likely to have anisometropia or combined mechanism as the cause of amblyopia (63% versus 43%), and they had more hyperopia in the amblyopic eye (mean spherical equivalent 5.39 diopters (D) versus 4.24 D) than those in the weaning group.

At the 10-week primary outcome examination, amblyopic eye visual acuity improved 2 or more lines from enrollment in 3 (11%) of the 27 subjects in the intensive treatment group and 6 (22%) of the 27 subjects in the weaning group (difference in proportions = -10%, 95% CI -30% to +9%, Table 3). Improvement in amblyopic eye visual acuity averaged 0.5 logMAR lines in both groups (treatment group difference in mean logMAR lines adjusted for baseline visual acuity = 0.0, 95% CI, -0.7 to +0.7, Table). After adjusting for gender, cause of amblyopia, amblyopic eye refractive error, and visual acuity testing method (Amblyopia Treatment Study HOTV[®] testing protocol³ vs Electronic Early Treatment Diabetic Retinopathy Study[®] testing protocol⁴), results were similar (data not shown).

Comment

For children with amblyopia who have already stopped improving with 6 hours of prescribed daily patching or daily atropine, we found that an intensive “final push” of combined treatment of patching and atropine did not produce a better visual acuity outcome after 10 weeks compared with a control group in which treatment was gradually discontinued. In spite of our small sample size, it is unlikely that a meaningful effect was missed, since both the upper and the lower limits of the 95% confidence interval for the mean difference between treatment groups were less than one line.

This study evaluated a select group of children with mild residual amblyopia (acuity of 20/32 to 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.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Access to Data

The authors had full access to all of the data in the study, and I take responsibility for the integrity of the data and the accuracy of the data analysis.

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Table

Amblyopic Eye Visual Acuity at the 10-week Primary Outcome Exam*

	10-week Primary Outcome Exam	
	Intensive Treatment N = 27	Weaning N = 27
	n (%)	n (%)
Change from Baseline to 10 weeks		
≥ 3 lines worse	0	1 (4%)
2 to < 3 lines worse	1 (4%)	0
1 to < 2 lines worse	2 (7%)	4 (15%)
Within 1 logMAR line	12 (44%)	8 (30%)
1 to < 2 lines better	9 (33%)	8 (30%)
2 to < 3 lines better	3 (11)	5 (19%)
≥ 3 lines better	0	1 (4%)
Mean (SD) lines change	0.56 (0.96)	0.53 (1.5)
95% confidence interval	(0.18 to 0.93)	(−0.04 to 1.1)
Two or more lines improved**	3 (11%)	6 (22%)
Difference between groups (95% confidence interval)	Intensive minus Weaning*** −10% (−30% to +9%)	
Distribution of Visual Acuity at 10 weeks		
20/125	0	1 (4%)
20/100	0	0
20/80	1 (4%)	1 (4%)
20/63	1 (4%)	4 (15%)
20/50	4 (15%)	0
20/40	13 (48%)	9 (33%)
20/32	7 (26%)	7 (26%)
20/25	1 (4%)	3 (11%)
20/20	0	2 (7%)
20/16	0	0
Mean (SD) logMAR	0.30 (0.10)	0.29 (0.18)
Snellen Equivalent	20/40	20/40 ⁺¹
Mean difference between treatment groups in logMAR visual acuity adjusted for baseline acuity (95% confidence interval).	Intensive minus Weaning +0.00 (−0.07, +0.07)	

SD= standard deviation; logMAR = logarithm of the minimum angle of resolution

* Visual acuity testers were masked for the primary outcome exam.

** P = 0.30 for difference between treatment groups in proportion of subjects 2 or more lines improved from logistic regression controlling for baseline acuity. One subject missing primary outcome exam in weaning group considered to have not improved 2 or more lines for analyses.

*** Negative difference favors the Weaning group.