A Comparison of Atropine and Patching Treatments for Moderate Amblyopia by Patient Age, Cause of Amblyopia, Depth of Amblyopia, and Other Factors

The Pediatric Eye Disease Investigator Group

Objective: To assess whether the relative treatment effect of patching compared with atropine for moderate amblyopia varies according to patient age, cause of amblyopia or depth of amblyopia, and initial number of patching hours prescribed.

Design: Multicenter, randomized clinical trial.

Participants: Four hundred nineteen children younger than 7 years of age with amblyopia in the range of 20/40 to 20/100.

Methods: Patients were assigned randomly to receive treatment with either patching or atropine and followed up for 6 months.

Primary Outcome Measure: Single-surrounded HOTV optotype visual acuity in the amblyopic eye after 6 months.

Results: Improvement in the amblyopic eye visual acuity was slightly greater in the patching group compared with the atropine group in all subgroups based on patient characteristics. The relative treatment effect did not vary with age ($P = 0.84$), cause of amblyopia ($P = 0.68$), or baseline amblyopic eye acuity ($P = 0.59$). Patients with acuity of 20/80 to 20/100 who were prescribed 10 or more hours a day of patching showed a more rapid improvement in acuity than did patients prescribed a lesser amount of patching ($P = 0.01$) or than did patients in the atropine group ($P < 0.001$), but by 6 months, the differences were not significant ($P = 0.47$ and 0.15, respectively).

Conclusions: A beneficial effect of both patching and atropine is present throughout the age range of 3 to younger than 7 years old and the acuity range of 20/40 to 20/100. Patients with acuity of 20/80 to 20/100 improve faster when a greater number of hours of patching is prescribed, but by 6 months, the amount of improvement is not related to the number of hours of patching initially prescribed. *Ophthalmology 2003;110:1632–1638 © 2003 by the American Academy of Ophthalmology.*

Amblyopia is the most common cause of monocular visual impairment in both children and young and middle-aged adults.[1–3] Patching of the sound eye and, less commonly, atropine drops for the sound eye have been the mainstays of therapy.

Factors that have been suggested to be associated with a poorer response to amblyopia treatment include older age, worse visual acuity, and strabismus as the cause of amblyopia.[4–7] Retrospective case reports have suggested that pharmacologic penalization may be less effective than occlusion or even ineffective for children with poorer amblyopic eye acuity.[8] Previous randomized studies comparing pharmacologic penalization with occlusion therapy have been too small to assess whether there are differences in treatment response according to patient characteristics (eg., age, cause of amblyopia, depth of amblyopia).[9,10]

We conducted a randomized trial comparing patching with atropine as treatments for moderate amblyopia (20/40 to 20/100) in children younger than 7 years. As previously reported, we found that substantial improvement in the visual acuity of the amblyopic eye occurred with both the patching and the atropine treatment regimens. Improvement was more rapid in the patching group, but by 6 months, the difference in acuity between treatment groups was small (approximately one third of a line).[11] Although both treatments were well tolerated, atropine was the favored treatment on a questionnaire completed after the first 5 weeks of treatment. More patients in the atropine group than in the patching group had reduced acuity in the sound eye at 6 months. However, in nearly all cases with follow-up information after the first 6 months, visual acuity in the sound eye returned to its prestudy level. In this report, we evalu-

Originally received: September 6, 2002.
Accepted: January 28, 2003. Manuscript no. 220683.

Writing committee members are listed in the Appendix. Participating investigators can be found using reference 11.

Supported by a cooperative agreement from the National Eye Institute, Bethesda, Maryland (grant no.: EY11751).

Reprint requests to PEDIG Data Coordinating Center, JAEB Center for Health Research, 15310 Amberly Drive, Suite 350, Tampa, FL 33613.

ISSN 0161-6420/03/$–see front matter
doi:10.1016/S0161-6420(03)00500-1

Table 1. Visual Acuity in Amblyopic Eye at 6 Months Stratified by Baseline Acuity in Amblyopic Eye

	n	Mean 6-Month Visual Acuity, logMAR (Snellen*)	Mean Lines Change from Baseline	Treatment Success†
All patients				
Atropine	194	0.25 ($20/30^{-2}$)	2.84	74%
Patching	208	0.21 (20/30)	3.16	79%
Visual acuity at baseline,‡ logMAR (Snellen equivalent)				
0.70 (20/100)				
Atropine	45	0.36 ($20/50^{+2}$)	3.42	80%
Patching	47	0.33 ($20/40^{-1}$)	3.70	74%
0.60 (20/80)				
Atropine	51	0.28 ($20/40^{+1}$)	3.22	71%
Patching	40	0.24 ($20/30^{-2}$)	3.65	80%
0.50 (20/62)				
Atropine	35	0.23 ($20/30^{-1}$)	2.71	54%
Patching	55	0.20 (20/30)	3.02	73%
0.40 (20/50)				
Atropine	38	0.17 ($20/30^{-2}$)	2.32	79%
Patching	47	0.13 ($20/25^{-1}$)	2.74	81%
0.30 (20/40)				
Atropine	24	0.12 ($20/25^{-1}$)	1.79	92%
Patching	19	0.08 ($20/25^{+1}$)	2.21	100%

Seventeen patients without a 6-month exam are not included (seven in patching group and 10 in atropine group).
*Estimated from logMAR score, where one letter = 0.02 logMAR; odd logMAR scores rounded down.
†Treatment success defined as outcome exam with acuity of ≥20/30, three lines of improvement from baseline, or both (crossovers to alternate treatment considered treatment failures).
‡One patient (atropine group) with baseline amblyopic eye visual acuity of 20/125 not included. $P = 0.59$ for interaction between baseline visual acuity and treatment group.
logMAR = logarithm of the minimum angle of resolution.

ated whether the relative treatment benefit comparing atropine and patching differs related to baseline patient characteristics such as age, cause of amblyopia, and depth of amblyopia. In addition, we compared the response to differing initial numbers of hours of daily patching.

Methods

The study protocol has been detailed in prior publications[11,12] and is summarized below. The study was conducted by the Pediatric Eye Disease Investigator Group at 47 clinical sites and was supported through cooperative agreements with the National Eye Institute of the National Institutes of Health. Institutional review boards approved the protocol and informed consent forms, and the parent or guardian (referred to subsequently as "parent") of each study patient gave written informed consent.

The major eligibility criteria for the trial included age younger than 7 years and ability to complete the study's visual acuity testing protocol[13] (which effectively created a lower age limit of approximately 3 years), visual acuity in the amblyopic eye ≤ 20/40 and ≥ 20/100, intereye acuity difference ≥ 3 logarithm of the minimum angle of resolution (logMAR) lines, the presence of or a history of an amblyogenic factor meeting study-specified criteria for strabismus or anisometropia, the wearing of optimal spectacle correction for a minimum of 4 weeks at the time of enrollment, and no more than 2 months of amblyopia treatment in the prior 2 years. Each patient was randomly assigned to treatment with either patching or atropine. Protocol-specified follow-up visits were conducted after 5, 16, and 26 weeks. Visual acuity was measured at baseline and at each follow-up visit with the Amblyopia Treatment Study Visual Acuity Testing Protocol.[13,14]

For the patching group, each patient was prescribed daily patching of the sound eye for a minimum of 6 hours per day and up to full-time (all or all but one waking hours) at investigator discretion. If by 4 months the acuity in the amblyopic eye had not reached 20/30 or improved from baseline by three or more lines, then full-time patching was prescribed (if not previously prescribed). For patients who responded well to treatment (acuity 20/30 or at least a three-line improvement from baseline), the amount of patching could be reduced at investigator discretion, but was required to be at least 7 hours per week as long as the acuity in the amblyopic eye was one or more lines worse than the acuity in the sound eye.

For the atropine group, each patient was prescribed one drop of atropine 1% in the sound eye per day. If by 4 months the acuity in the amblyopic eye had not reached 20/30 or improved from baseline by three or more lines, then the spectacle lens for the sound eye was replaced with a plano lens (for patients wearing spectacles). For patients who responded well to treatment (acuity 20/30 or at least a three-line improvement from baseline), the atropine dosage could be reduced at investigator discretion but was required to be at least 2 days per week as long as the acuity in the amblyopic eye was one or more lines worse than the acuity in the sound eye.

Statistical Methods

The primary outcome was the 6 month amblyopic eye logMAR visual acuity score. A prespecified secondary outcome (*treatment success*) was defined as a 6-month acuity that was ≥ 20/30, improved from baseline by three or more lines, or both. A patient was classified as a *treatment failure* if the success criteria were not met or if the nonassigned treatment was received for at least 1 week (i.e., a patient in the atropine group received patching or a patient in the patching group received atropine).

Table 2. Visual Acuity in the Amblyopic Eye at 6 Months According to Baseline Patient Characteristics

Baseline Characteristic	n (Patching, Atropine)	Mean Lines Improvement from Baseline		Treatment Success, %*		P Value for Interaction†
		Patching	*Atropine*	*Patching*	*Atropine*	
All patients	(208, 194)	3.16	2.84	79%	74%	
Gender						0.70/0.48
Male	(108, 104)	3.16	2.80	81%	73%	
Female	(100, 90)	3.16	2.89	77%	76%	
Race						0.47/0.33
White	(168, 165)	3.17	2.90	79%	76%	
Other	(40, 29)	3.13	2.52	80%	66%	
Age (yrs)						0.84/0.21
<5	(74, 76)	3.20	2.87	82%	70%	
≥5	(134, 118)	3.13	2.82	77%	77%	
Cause of amblyopia‡						0.68/0.83
Strabismus	(80, 73)	3.00	2.90	79%	74%	
Anisometropia	(81, 68)	3.19	2.91	83%	76%	
Strabismus and Anisometropia	(46, 49)	3.37	2.65	72%	73%	
Prior therapy for amblyopia§						0.13/0.05
Yes	(55, 51)	3.25	2.53	82%	63%	
No	(153, 143)	3.12	2.95	78%	78%	
Refractive error in sound eye (spherical equivalent)						0.70/0.91
<+3.00	(134, 104)	3.14	2.82	79%	75%	
≥+3.00	(74, 90)	3.19	2.87	78%	73%	

Seventeen patients without a 6-month exam are not included (7 in patching group and 10 in atropine group).
*Treatment success defined as outcome exam with acuity of ≥20/30, three-line improvement from baseline, or both (crossovers to alternate treatment considered treatment failures).
†The *P* values are for the interaction between the characteristic and treatment from a model that included baseline amblyopic eye acuity, treatment group, and the characteristic. The first *P* value is from an analysis of covariance model with the 6-month amblyopic eye acuity as the dependent variable, and the second *P* value is from a generalized linear model with treatment success as the dependent variable.
‡Five patients with indeterminate cause for amblyopia not included (one patching, four atropine).
§For 92% of patients with prior amblyopia treatment, patching was the prior treatment.

The modifying effects of baseline patient characteristics on the treatment group differences in amblyopic eye acuity at 6 months were assessed by including interaction terms in analysis of covariance models (logMAR visual acuity score as dependent variable) and by generalized linear models (treatment success as dependent variable) adjusted for baseline acuity, with a separate model for each patient characteristic. For continuous variables (e.g., age), the interaction term used the continuous form of the variable; strata for the variable are provided in tables for ease of interpretation.

The treatment response according to the number of hours of patching prescribed at baseline was evaluated in an exploratory analysis. The patching group was divided into two subgroups based on the initial number of hours of daily patching that were prescribed (6 to 8 hours and 10 or more hours). The subgroup prescribed daily patching of 10 or more hours was then compared in separate analysis of covariance models with the subgroup prescribed 6 or 8 daily patching hours and with the atropine group at the three protocol-specified visits (5 weeks, 16 weeks, and 6 months).

All analyses followed the intention-to-treat principle (i.e., the treatment group data were based on the randomization assignments, not on the actual treatment received or whether the treatment protocol was followed). Data were not imputed for the 17 patients who left the study before the 6-month exam. All reported *P* values are two tailed.

Results

The trial enrolled 419 patients, with 215 assigned to the patching group and 204 assigned to the atropine group. The 6-month outcome exam was completed by 208 patients (97%) in the patching group and by 194 patients (95%) in the atropine group. The average age of the patients was 5.3 years; 47% were female and 83% were white. The mean visual acuity in the amblyopic eye at enrollment was approximately 20/60, with a mean difference in acuity between eyes of 4.4 lines. The identified amblyogenic factor was strabismus in 159 (38%), anisometropia in 155 (37%), and both strabismus and anisometropia in 100 (24%). Five enrolled patients did not meet the study criteria for either strabismus or anisometropia. Patient characteristics were well balanced between the two treatment groups.[11] Additional baseline data were reported previously.[12]

Treatment Group Differences According to Patient Characteristics

The relative treatment effect comparing the two treatment groups was similar across the range of visual acuities included in the trial (20/40 to 20/100; *P* value for interaction = 0.59). At each level of baseline visual acuity, a slightly greater improvement in the 6-month visual acuity was present consistently in the patching group compared with the atropine group (Table 1).

The relative treatment effect was similar in males and females (*P* value for interaction = 0.70) and did not vary with age (*P* value

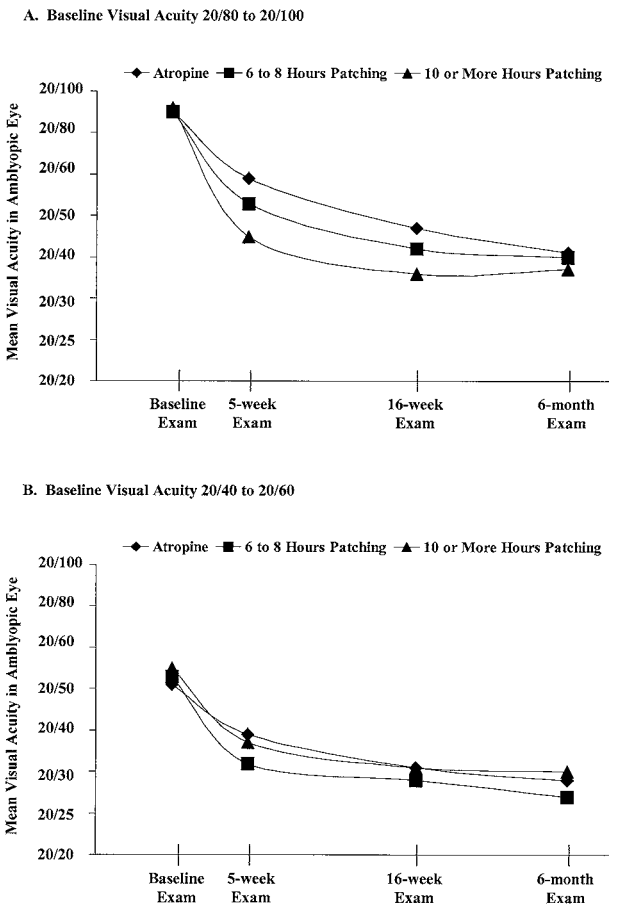

Figure 1. Mean visual acuity in the amblyopic eye at the 5-week, 16-week, and 6-month examination for (**A**) patients with baseline acuity in the amblyopic eye 20/80 to 20/100, and (**B**) patients with baseline acuity in the amblyopic eye 20/40 to 20/60. For the atropine, 6–8 hours patching, and 10 or more hours patching treatment groups: (**A**) n at baseline, (101, 52, and 39); n at 5 weeks, (100, 50, and 37); n at 16 weeks, (96, 49, and 36); and n at 6 months, (97, 50, and 37); and (**B**) n at baseline, (103, 104, and 20); n at 5 weeks, (99, 102, and 20); n at 16 weeks, (97, 96, and 19); and n at 6 months, (97, 101, and 20).

for interaction = 0.84) or with race (P value for interaction = 0.47).

The treatment effect also was unrelated to whether the cause of amblyopia was strabismus, anisometropia, or both combined (P value for interaction = 0.68; Table 2). In the combined-mechanism subgroup, although the mean improvement with patching was numerically greater than the mean improvement with atropine, the proportions meeting the criteria for treatment success were similar. These apparently contradictory results appeared, at least in part, to be related to a treatment group imbalance in baseline acuity in this subgroup. Among the patients with combined-mechanism amblyopia, a greater number of patients in the patching group had a baseline acuity of 20/100, and a greater number of patients in the atropine group had a baseline acuity of 20/40.

The relative treatment effect also did not vary based on whether the patient had been previously treated for amblyopia (P value for interaction = 0.13) or on refractive error in the sound eye (P value for interaction = 0.70; Table 2).

Treatment Group Differences According to Patching Hours Prescribed

The initial number of patching hours was prescribed based on an investigator's usual practice with the stipulation that a minimum of 6 hours per day be prescribed. This investigator discretion resulted in patients with 20/80 or 20/100 baseline acuity being prescribed 10 or more hours per day of patching more often than were patients with 20/40 to 20/60 acuity ($P < 0.001$). To account for this selection bias in the intensity of patching treatment prescribed, analyses were performed for two strata based on the baseline amblyopic eye acuity (20/80 to 20/100 and 20/40 to 20/60).

After 5 weeks of treatment, patients prescribed 10 or more hours of patching per day had greater improvement in visual acuity compared with patients in the atropine group ($P < 0.001$) and showed a trend toward greater improvement compared with patients prescribed 6 or 8 hours per day ($P = 0.10$). The benefit of the more intensive patching was most pronounced when baseline acuity was 20/80 to 20/100 ($P < 0.001$ compared with atropine and $P = 0.01$ compared with 6 to 8 hours of daily patching). As can be seen in Figure 1 and Table 3, the differences between the three groups narrow with further follow up such that by 6 months, the differences among the groups are small.

Discussion

Substantial improvement in the visual acuity of the amblyopic eye occurred with both the patching and the atropine treatment regimens. After 6 months, the difference in mean logMAR acuity between treatment groups was small (approximately one third of a line). The effects of the treatments were remarkably consistent across the 3 to younger than 7-year age range and the 20/40 to 20/100 acuity range and did not vary based on whether the cause of the amblyopia was related to strabismus, anisometropia, or both. We also evaluated gender, race, and refractive error of the sound eye and found a consistent relative treatment effect in all subgroups. However, the number of nonwhite patients in the trial was too few for a meaningful statistical assessment.

The beneficial effect of atropine at the lower (worse) end of the visual acuity range is an important finding. Retrospective case reports have suggested that pharmacologic penalization may be less effective than occlusion or even ineffective for children with poorer amblyopic eye acuity.[8] However, our results indicate that atropine was just as effective when acuity was 20/100 as when acuity was 20/40. This finding points to the need for a future study to assess the effect of atropine at acuity levels worse than 20/100.

During the design phase of the trial, we postulated that compared with patching, atropine may be more successful for the older amblyopic patient than for the younger patient because of better relative compliance with atropine at the older age.[8] Such a difference was not found in the trial; rather, the relative benefit of the two treatments was of similar magnitude over the age range studied.

Previously, we reported that although the treatment group differences at 6 months were small, patching produced a more rapid improvement in acuity than did atropine. Further analyses reported herein demonstrated that the effect of more rapid improvement was greatest for patients whose initial visual acuity was 20/80 to 20/100 and who

Table 3. Amblyopic Eye Visual Acuity Comparing 10 or More Hours of Daily Patching with 6 to 8 Hours of Daily Patching and with Atropine Treatment

	Baseline		5-Week Exam		16-Week Exam			6-Month Exam					
	n	*logMAR Acuity (mean)*	*logMAR Acuity (mean)*	*Lines Change from Baseline (mean)*	*P* Value*	*logMAR Acuity (mean)*	*Lines Change from Baseline (mean)*	*P* Value*	*logMAR Acuity (mean)*	*Lines Change from Baseline (mean)*	*P* Value*	*Success†*	*P‡ Value*
Baseline acuity 20/80 to 20/100													
Atropine	101	0.65	0.49	1.55	<0.001	0.37	2.79	<0.001	0.31	3.35	0.15	75%	0.74
6 to 8 hours patching	52	0.65	0.43	2.18	0.01	0.32	3.33	0.04	0.30	3.56	0.47	80%	0.58
≥10 hours patching	39	0.66	0.35	3.05		0.26	4.00		0.27	3.84		73%	
Baseline acuity 20/40 to 20/60													
Atropine	103	0.41	0.29	1.18	0.19	0.21	2.06	0.62	0.18	2.33	0.92	73%	0.88
6 to 8 hours patching	104	0.43	0.22	2.01	0.29	0.18	2.46	0.55	0.14	2.85	0.13	82%	0.37
≥10 hours patching	20	0.45	0.27	1.80		0.21	2.37		0.20	2.45		70%	

For patients with baseline acuity 20/80 to 20/100, in the atropine, 6–8 hours patching, and 10 or more hours patching treatment groups: n at 5 weeks, (100, 50, 37); n at 16 weeks, (96, 49, 36); and n at 6 months, (97, 50, 37). For patients with baseline acuity 20/40 to 20/60: n at 5 weeks, (99, 102, 20); n at 16 weeks, (97, 96, 19); and n at 6 months, (97, 101, 20).

**P* value for difference in mean logarithm of the minimum angle of resontion acuity score between each treatment subgroup compared with ≥10 hours patching subgroup from analysis of covariance model in which the logarithm of the minimum angle of resontion acuity scores were adjusted for baseline acuity.

†Success defined as outcome examination with acuity of ≥20/30, three-line improvement from baseline, or both (crossovers to alternate treatment considered treatment failures).

‡*P* value for difference in success proportions between each treatment subgroup compared with ≥10 hours patching subgroup from generalized model adjusted for baseline acuity.

logMAR = logarithm of the minimal angle of resolution.

were prescribed full-time or nearly full-time daily patching. This finding has potential importance for the clinician who is weighing the pros and cons of patching and atropine therapies. However, it must be viewed with some caution because as a secondary analysis, the probability that it is a chance finding is increased. As noted earlier, we attempted to control for the selection bias that was present related to the number of hours of patching prescribed; however, some bias could still be present, particularly within the baseline acuity stratum of 20/40 to 20/60 where only 1 of the 19 patching patients with baseline acuity of 20/40 was prescribed 10 or more hours of daily patching. We currently are performing additional randomized trials to assess specifically the outcome with different patching regimens.

The amount of patching that is believed necessary to improve vision varies widely among pediatric eye care providers, ranging from all waking hours to just minutes per day. Only a few reports have evaluated the difference between full (or nearly full) and part-time occlusion, when the groupings were not established by an assessment of patient compliance. Flynn et al[7] suggested that the success rates were the same for part-time and full-time occlusion therapy. Their analysis, based solely on reported outcomes in 23 studies, would not have identified the more rapid improvement seen with 10 or more hours of daily occlusion in this study. Cleary[15] reported that full-time occlusion produced a greater improvement in visual acuity and reduction in interocular difference than part-time occlusion, when the acuity outcome was measured at 6 months. The interpretation of these studies, as well as our own, is somewhat limited because the analyses are based on the prescribed occlusion dosage, rather than the amount of patching actually achieved. An analysis of dose effect from actual episodes of patching must await the widespread availability of dose-monitoring devices.[16,17]

In summary, both patching and atropine are effective initial treatments for amblyopia throughout the age range of 3 to younger than 7 years and the acuity range of 20/40 to 20/100. Patients with acuity of 20/80 to 20/100 improve faster when a greater number of hours of patching is prescribed, but after 6 months, the improvement is not significantly greater than that occurring with a lesser number of hours of patching or with atropine. For the clinician weighing the pros and cons of patching versus atropine as an initial therapy for a child with amblyopia who is within this age and acuity range, our results indicate that age, depth of amblyopia, and cause of amblyopia are not important factors to consider. In some cases, parent or even child preference may be the overriding factor in deciding which treatment to prescribe.

References

1. Ederer F, Krueger DE. Report on the National Eye Institute's Visual Acuity Impairment Survey pilot study. Washington, DC: National Eye Institute, 1984:81–4.
2. Simons K. Preschool vision screening: rationale, methodology and outcome. Surv Ophthalmol 1996;41:3–30.
3. Attebo K, Mitchell P, Cumming R, et al. Prevalence and causes of amblyopia in an adult population. Ophthalmology 1998;105:154–9.
4. Hiscox F, Strong N, Thompson JR, et al. Occlusion for amblyopia: a comprehensive survey of outcome. Eye 1992;6: 300–4.
5. Woodruff G, Hiscox F, Thompson JR, Smith LK. Factors affecting the outcome of children treated for amblyopia. Eye 1994;8:627–31.
6. Newman DK, Hitchcock A, McCarthy H, et al. Preschool vision screening: outcome of children referred to the hospital eye service. Br J Ophthalmol 1996;80:1077–82.
7. Flynn JT, Schiffman J, Feuer W, Corona A. The therapy of amblyopia: an analysis of the results of amblyopia therapy utilizing the pooled data of published studies. Trans Am Ophthalmol Soc 1998;96:431–50: discussion 450–3.
8. Repka MX, Ray JM. The efficacy of optical and pharmacological penalization. Ophthalmology 1993;100:769–74.
9. Doran RMl, Yarde S, Starbuck A. Comparison of treatment methods in strabismic amblyopia. In: Campos EC, ed. Strabismus and Ocular Motility Disorders. London: Macmillan press, 1990:51–9 chap. 5.
10. Foley-Nolan A, McCann A, O'Keefe M. Atropine penalisation versus occlusion as the primary treatment for amblyopia. Br J Ophthalmol 1997;81:54–7.
11. The Pediatric Eye Disease Investigator Group. A randomized trial of atropine vs. patching for treatment of moderate amblyopia in children. Arch Ophthalmol 2002;120:268–78.
12. The Pediatric Eye Disease Investigator Group. The clinical profile of moderate amblyopia in children younger than age 7. Arch Ophthalmol 2002;120:281–7.
13. The Pediatric Eye Disease Investigator Group, Holmes JM, Beck RW, Repka MX, et al. The amblyopia treatment study visual acuity testing protocol. Arch Ophthalmol 2001;119:1345–53.
14. Moke PS, Turpin AH, Beck RW, et al. Computerized method of visual acuity testing: adaptation of the Amblyopia Treatment Study visual acuity testing protocol. Am J Ophthamol 2001;132:903–9.
15. Cleary M. Efficacy of occlusion for strabismic amblyopia: can an optimal duration be identified? Br J Ophthalmol 2000;84: 572–87.
16. Moseley MJ, Fielder AR, Irwin M, et al. Effectiveness of occlusion therapy in ametropic amblyopia: a pilot study. Br J Ophthalmol 1997;81:956–61.
17. Simonsz HJ, Polling JR, Voorn R, et al. Electronic monitoring of treatment compliance in patching for amblyopia. Strabismus 1999;7:113–23.

Appendix

Writing Committee

Michael X. Repka, MD, Roy W. Beck MD, PhD, Raymond T. Kraker, MSPH, Jonathan M. Holmes, BM, BCh, Eileen E. Birch, PhD, Stephen R. Cole, PhD, C. Gail Summers, MD, David T. Wheeler, MD, Susan A. Havertape, Susanna M. Tampkins, OD

Discussion
by
Burton J. Kushner, MD

In this secondary paper, the authors continue their investigation into the treatment of the amblyopia with atropine. The Pediatric Eye Disease Investigator Group (PEDIG) is to be commended for bringing good science to the investigation of this subject. This present study investigates the relative influence of age, cause of amblyopia, and the initial depth of amblyopia on the efficacy of atropine. In short, they found that these factors did not have a significant influence. In this study, as well as the primary outcome study,[1] the authors concluded that atropine and patching produce improvement of similar magnitude, and that both are appropriate methods of treatment. They suggested that in some cases, "parent, or even child preference, may be the overriding factor in deciding which treatment to prescribe."

These conclusions need to be viewed in light of some important issues. This study, like all good studies, had a predetermined, but arbitrary, outcome question. It asked which treatment method had a higher percentage of patients achieving a final visual acuity of 20/30 by 6 months after treatment began. However, this outcome question was not the only one that the investigators might have asked, nor was it necessarily the best one. Patients, of course, do not necessarily ask which therapy has a better likelihood of achieving 20/30 vision after 6 months of treatment. They simply want to know, "Which treatment is better?" When one asks that question, other important factors come into play.

The data show that 56% of the patients undergoing patching achieved of the targeted acuity of 20/30 by the 5-week examination. This compares with only 33% of the patients receiving atropine, and this difference is significant ($P < 0.0001$). The authors gloss over this difference by stating the results even out by the 6-month examination. However, this unduly minimizes the importance of this issue. The difference between a patient being cured of amblyopia after 6 months of treatment, versus only 5 weeks, can mean a difference of four or five additional trips to the doctor's office. This translates into more time off work, more inconvenience, greater expense, a prolongation of the difficulties that may be encountered with treatment, and more frustration for parent and child.

Similarly, the study design arbitrarily uses a final visual acuity of 20/30 or better for the definition of a successful outcome. Had the authors chosen a higher level of visual acuity as their criteria for success, patching clearly produced better results. Forty percent of the patching patients achieved a final visual acuity of 20/25 or better, verses only 28% of the atropine patients. This difference was also significant ($P < 0.01$).

From the Department of Ophthalmology and Visual Sciences, University of Wisconsin, Madison, Wisconsin.

Correspondence to Burton J. Kushner MD, Department of Ophthalmology and Visual Sciences, University of Wisconsin, 2870 University Avenue, Suite 206, Madison, WI 53705.