The Clinical Profile of Moderate Amblyopia in Children Younger Than 7 Years

The Pediatric Eye Disease Investigator Group

Objectlve: To describe the demographic and clinical characteristics of a cohort of children with moderate amblyopia participating in the Amblyopia Treatment Study 1, a randomized trial comparing atropine and patching.

Methods: The children enrolled were younger than 7 years and had strabismic, anisometropic, or combined strabismic and anisometropic amblyopia. Visual acuity, measured with a standardized testing protocol using single-surround HOTV optotypes, was 20/40 to 20/100 in the amblyopic eye, with an intereye acuity difference of 3 or more logMAR lines. There were 419 children enrolled, 409 of whom met these criteria and were included in the analyses.

Results: The mean age of the 409 children was 5.3 years. The cause of the amblyopia was strabismus in 38%, anisometropia in 37%, and both strabismus and anisometropia in 24%. The mean visual acuity of the amblyopic eyes (approximately 20/60) was similar among the strabismic, anisometropic, and combined groups (P= .24), but visual acuity of the sound eyes was worse in the strabismic group compared with the anisometropic group (P<.001). For the patients randomized into the patching group, 43% were initially treated for 6 hours per day, whereas 17% underwent full-time patching. Patients with poorer visual acuity in the amblyopic eye were prescribed more hours of patching than patients with better acuity (P=.003).

Conclusions: In the Amblyopia Treatment Study 1, there were nearly equal proportions of patients with strabismic and anisometropic amblyopia. A similar level of visual impairment was found irrespective of the cause of amblyopia. There was considerable variation in treatment practices with regard to the number of hours of initial patching prescribed.

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AMBLYOPIA IS the most common cause of visual impairment in children. The prevalence of amblyopia in children has been estimated at between 1% and 4%.[1-4] Most cases are associated with eye misalignment, usually esotropia in infancy or early childhood.[5,6] Less frequently, anisometropia (difference in refractive error between the two eyes) or a combination of strabismus and anisometropia are causally associated with amblyopia.

The Amblyopia Treatment Study 1 (ATSl) is a randomized, controlled, single-masked multicenter clinical trial designed to compare the visual acuity improvement achieved using patching therapy with adhesive patches with pharmacological penalization using topical atropine sulfate 1% drops. Children younger than 7 years with moderate amblyopia were enrolled at both community-based and university-based practices throughout North America by the Pediatric Eye Disease Investigator Group. In this article, we describe the demographic and clinical characteristics of the cohort of patients enrolled into the ATSI.

From the Jaeb Center for Health Research, Tampa, Fla. A list of the writing committee members of the Pediatric Eye Disease Investigator Group appears on page 287.

RESULTS

Between April 1999 and April 2001, 419 patients were enrolled at 47 sites (10 patients were ineligible and were not included in the analyses, as indicated in the "Methods" section). There were 188 patients enrolled at 16 community-based ophthalmology practices, 183 patients at 24 departments of ophthalmology, and 48 patients at 7 schools or colleges of optometry.

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The mean± SD age of the 409 patients was 5.3± I.I years, ranging from 2.6 to 6.9 years. Forty-six percent were girls. The racial distribution was 83% white, 6% African American, 6% Hispanic, 2% Asian, and 3% mixed or other. Of these patients, 73% had received no prior treatment for ambly

PATIENTS AND METHODS

The study was supported through a cooperative agreement with the National Eye Institute of the National Institutes of Health (Bethesda, Md) and conducted at 47 clinical sites **in** North America. Institutional review boards approved the protocol and informed consent forms. The parent or guardian of each study patient gave written informed consent. An independent data and safety monitoring committee provided study oversight.

PATIENT SELECTION

Eligibility and exclusion criteria for enrollment are listed in Table I. Eligibility testing included the measurement of visual acuity in both eyes using the ATS visual acuity testing protocol (see "Measurement of Visual Acuity"), a cycloplegic refraction, an ocular examination, and a sensorimotor evaluation. Procedures were performed according to the investigator's usual routine except for the visual acuity testing protocol. Visual acuity testing was performed within the 7 days prior to randomization, whereas the remainder of the examination was completed within 2 months prior to randomization.

STUDY DEFINITIONS OF AMBLYOPIA

For each patient, amblyopia was classified as either strabismic, refractive/anisometropic, or combined-mechanism to indicate the presumptive cause of amblyopia. *Strabismic amblyopia* was defined as amblyopia (1) in the presence of either a heterotropia at distance and/or near fixation or a history of strabismus surgery (or botulinum toxin injection), and (2) in the absence of refractive error meeting the criteria for combined-mechanism amblyopia. *Refractive/anisometropic amblyopia* (subsequently referred to as *anisometropic amb!yopia)* was defined as amblyopia in the presence of anisometropia that was 0.50 diopter (D) or more in spherical equivalent or a 1.50 D or greater difference in astigmatism in any meridian that persisted after at least 4 weeks of spectacle correction, with no measurable heterotropia at distance or near fixation. *Combined-mechanism amblyopia* was defined as amblyopia in the presence of (1) either a heterotropia at distance and/or near fixation or a history of strabismus surgery (or botulinum toxin injection), and (2) anisometropia that was 1.00 D or more in spherical equivalent or a 1.50 D or greater difference in astigmatism in any meridian that persisted after at least 4 weeks of spectacle correction.

The refractive error criteria for these classifications were set arbitrarily based on the consensus opinion of the investigator group. These criteria must be viewed in the context of a patient diagnosed as having amblyopia who has at least a 3-line decrease **in** visual acuity **in** the amblyopic eye compared with the sound eye. Some of the patients classified as having anisometropic amblyopia may have had a small deviation of 8 D or less that was not detected during the examination. Different refractive criteria were used in the definitions of anisometropic amblyopia and combined-mechanism amblyopia, such that a patient with 0.50 or 0.75 D of spherical anisometropia and strabismus would be classified as strabismic rather than combined-mechanism. Small differences in refractive error between eyes are common, and in such cases the strabismus is likely the primary amblyogenic factor.

Table 1. Eligibility and Exclusion Criteria

Eligibility criteria
Age <7 y
Able to measure visual acuity with the Amblyopia Treatment Study visual acuity testing protocol, using single-surround HOTV optotypes*
Amblyopia associated with strabismus, refractive error/anisometropia, or both†
Visual acuity in the amblyopic eye :520/40 and 220/100
Visual acuity in the sound eye 220/40
Intereye acuity difference 2 3 logMAR lines
No more than 2 mo of amblyopia therapy in the past 2 y (any treatment more than 2 y ago was acceptable)
Refractive error corrected for at least 4 wk‡
Exclusion criteria
Presence of an ocular cause for reduced visual acuity
Prior intraocular surgery
Myopia (spherical equivalent of -0.50 diopters or more) in either eye
Down syndrome
Known skin reaction to patch or bandage adhesive, or allergy to atropine or other cycloplegics

*Excluded all patients younger than 2 years and many patients younger than 3 years.
†See "Methods" section for definition of each cause.
‡See "Methods" section for criteria for correction of refractive error.

opia, 24% had been previously treated with patching, 2% had been previously treated with atropine, and 1% had previously received some other form of amblyopia therapy.

The cause of amblyopia was strabismus in 38% of patients, anisometropia in 37%, and both strabismus and anisometropia (combined-mechanism) in 24%. The visual acuity in the amblyopic eye was 20/40 in 11%, 20/50 in 21%, 20/60 in 22%, 20/80 in 23%, and 20/100 in 23% (mean, 0.53 logMAR units [approximately 20/601). The interocular acuity difference ranged from 3 to 8 lines with a mean of 4.4 lines. There was no difference in mean visual acuity of the amblyopic eyes of patients who had received prior amblyopia therapy compared with those who had received no prior therapy (mean±SD, 0.53±0.13 logMAR units for both; P=.68).

The baseline characteristics of the cohort according to cause of amblyopia are summarized in **Table 2.** The patients with strabismic amblyopia were slightly younger at enrollment (mean age, 5.1 years) than the patients with anisometropic or combined-mechanism amblyopia (mean age, 5.4 years and 5.2 years, respectively; P= .04). Mean visual acuity in the amblyopic eye was similar for all 3 causes ofamblyopia (P=.24), but acuity in thesoundeyewasworse with strabismic amblyopia and best with pure anisometropic amblyopia even after adjusting for age, refractive er-

CORRECTION OF REFRACTIVE ERROR

For patients with strabismic amblyopia, refractive error was corrected according to the investigator's usual routine. Patients with anisometropic or combined-mechanism amblyopia were required to wear their current spectacle correction for at least 4 weeks when there was anisometropia of 1.00 D or more in spherical equivalent or a 1.50 D or greater meridional difference subject to the following guidelines: (1) full correction of anisometropia; (2) hyperopia of more than 3 D corrected by either prescribing the maximum-tolerated hyperopic correction or reducing the cycloplegic refraction by up to +1.50 D; and (3) correction of astigmatism in either eye of 1.50 D or greater (full correction of astigmatism preferred). If a patient was already wearing glasses, a new prescription was not necessary as long as (1) both the spherical equivalent and cylinder were within 0.50 D of fully correcting the anisometropia, and (2) the cylinder axis in both eyes was within 10° of the axis in the spectacles when the cylinder power was 1.00 D or greater (if cylinder power was < 1.00 D, a spectacle change was at the investigator's discretion).

MEASUREMENT OF VISUAL ACUITY

Visual acuity was measured in both eyes using the ATS visual acuity testing protocol administered by a study-certified vision tester. The testing protocol consists of the presentation of single-surround HOTV optotypes on the Baylor Video Acuity Tester (Medtronic Xomed Solan Ophthalmics, Jacksonville, Fla) in 4 steps: a screening phase, followed by a first-threshold determination (phase 1), reinforcement phase, and second-threshold determination (phase 2). In the screening phase, starting from 20/100, a single letter at each logMAR size is shown until one is missed. In phase 1, letters are shown starting 2 logMAR levels above the missed level in the screening phase to determine the smallest level at which 3 of 3 or 3 of 4 letters are correctly identified. In the reinforcement phase, to get the child with drifting attention back on track, 3 larger letters are shown starting 2 levels above the lowest correct level in phase 1. In phase 2, the child is retested at the last level missed in phase 1; if 3 of 3 or 3 of 4 are correctly identified, the test continues at the next-smallest level until a level is failed. The visual acuity score is the lowest level at which 3 of 3 or 3 of 4 presentations are correctly identified in phase 1 or phase 2.

DATA ANALYSIS

Ten patients enrolled in the study did not meet the eligibility criteria and were not included in the analyses (5 patients did not have a definable cause for amblyopia, 1 had a visual acuity in the amblyopic eye of 20/30, 1 had an acuity in the amblyopic eye of 20/125, and 3 had an interocular difference of only 2 logMAR lines).

Differences in baseline characteristics among subgroups based on cause of amblyopia and age at enrollment were assessed, as indicated, with X^2 tests as well as analysis of variance and analysis of covariance (with *t* tests used for subsequent 2-subgroup comparisons). The association between prior treatment for amblyopia and amblyopic eye visual acuity was assessed using a *t* test. The associations between the number of hours of daily patching prescribed at enrollment and visual acuity in the amblyopic eye, age at enrollment, practice type (community vs institution), and physician type (ophthalmologist vs optometrist) were evaluated with Kruskal-Wallis tests. Statistical analyses were performed using SAS statistical software (PC version 8.01; SAS Institute Inc, Cary, NC).

ror in the sound eye, and prior treatment of amblyopia (P<.001). This resulted in a smaller interocular acuity difference with strabismic amblyopia than with the other 2 causes (P<.001). Refractive error data for the 3 causes differed, consistent with the definitions for each cause. The magnitude of the anisometropia was greater when the amblyopia was due to anisometropia alone than when due to anisometropia combined with strabismus (P= .02). Among the patients with anisometropia, visual acuity in the amblyopic eye was worse when anisometropia was 3.00 D or more than when it was less than 3.00 D (mean visual acuity, 0.57 logMAR units [approximately 20/80] and 0.48 logMAR units [approximately 20/60], respectively; P<.001).

The baseline characteristics according to age at enrollment are listed in Table 3. Mean visual acuity in both the amblyopic and sound eyes was worse in the younger children (P=.005 and P<.001, respectively), but the intereye acuity difference did not vary with age (P=.59). The mean refractive errors of the amblyopic and sound eyes, as well as the anisometropia, varied little with age.

For patients randomized into the patching group, the initial number of daily patching hours was at the discretion of the investigator, with a minimum of 6 hours. Six or 8 hours per day were prescribed for 73% of the 212 patients, whereas 10 or more hours were prescribed for 27%. Although the number of hours prescribed had no consistent relationship to age (P= .50), it was related to the amblyopic eye acuity (P= .003). Among the 19 patients with an amblyopic eye acuity of 20/40, all were prescribed 6 or 8 hours per day of patching, whereas among the 49 patients with 20/100 amblyopic eye acuity, only 53% were prescribed 6 or 8 hours of patching per day. In contrast, full-time patching was prescribed for no patients with 20/40 amblyopic eye acuity and for 22% of patients with 20/100 acuity (Table 4). There was no difference in the number of patching hours prescribed by university-based investigators compared with community-based investigators (P=.36). However, on average the optometrist investigators prescribed fewer hours of patching than the ophthalmologist investigators (P= .01); only 4% of patients enrolled by an optometrist were initially prescribed 10 or more hours of patching per day, compared with 31% of patients enrolled by an ophthalmologist.

The ATS 1 was conducted using a simple protocol to compare the effectiveness of patching and topical atropine 1% solution as treatments for moderate amblyopia in children younger than 7 years. The study group investigators

Table 2. Baseline Characteristics According to Cause of Amblyopia*

		Cause of Amblyopia			Overall P †	2-Group Comparisons, P‡		
	Total (N = 409)	Strabismus (n = 156)	Anisometropia (n = 153)	Combined (n = 100)	Unadjusted (Adjusted for Age)	Strabismus vs Anisometropia	Strabismus vs Combined	Anisometropia vs Combined
Age, y								
< 3	7 (2)	2 (1)	3 (2)	2 (2)				
3 to < 4	60(15)	33 (21)	13 (9)	14 (14)				
4 to < 5	83 (20)	30 (19)	31 (20)	22 (22)				
5 to < 6	135 (33)	40 (26)	56 (37)	39 (39)				
6 to < 7	124 (30)	51 (33)	50 (33)	23 (23)				
Mean (SD), logMAR units	5.3 (1.1)	5.1 (1.2)	5.4 (1.0)	5.2(1.0)	.04	.02	.76	.06
Visual acuity (amblyopic eye)								
20/100	95 (23)	28 (18)	35 (23)	32 (32)				
20/80	95 (23)	44 (28)	31 (20)	20 (20)				
20/60	91 (22)	35 (22)	36 (24)	20 (20)				
20/50	84(21)	32 (21)	33 (22)	19 (19)				
20/40	44(11)	17 (11)	18 (12)	9 (9)				
Mean (SD), logMAR units	0.53 (0.13)	0.52 (0.13)	0.52 (0.13)	0.55 (0.14)	.24 (.27)	.95	.13	.13
Visual acuity (sound eye)								
20/40	38 (9)	24 (15)	6 (4)	8 (8)				
20/30	81 (20)	38 (24)	21 (14)	22 (22)				
20/25	113 (28)	57 (37)	30 (20)	26 (26)				
20/20	148(36)	36 (23)	75 (49)	37 (37)				
20/15	29 (7)	1 (0.6)	21 (14)	7 (7)				
Mean (SD), logMAR units	0.09 (0.11)	0.13 (0.10)	0.05 (0.10)	0.09 (0.11)	<.001 (<.001)	<.001	.001	.002
Intereye difference, lines								
3	128 (31)	66 (42)	37 (24)	25 (25)				
4	117 (29)	56 (36)	37 (24)	24 (24)				
5	78 (19)	20 (13)	33 (22)	25 (25)				
6	51 (12)	10 (6)	22 (14)	19 (19)				
7	30 (7)	4 (3)	20 (13)	6 (6)				
8	5 (1)	0	4 (3)	1 (1)				
Mean (SD), lines	4.4 (1.3)	3.9 (1.0)	4.8 (1.4)	4.6 (1.3)	<.001 (<.001)	<.001	<.001	.37
Refractive error (amblyopic eye), D§								
<1.00	19(5)	14 (9)	4 (3)	1 (1)				
1.00 to <2.00	33 (8)	23 (15)	9 (6)	1 (1)				
2.00 to <3.00	37 (9)	21 (13)	10 (7)	6 (6)				
3.00 to <4.00	60 (15)	27 (17)	25 (16)	8 (8)				
≥4,00	260 (64)	71 (46)	105 (69)	84 (84)				
Mean (SD), logMAR units	4.52 (2.09)	3.80 (2.18)	4.70 (1.98)	5.37 (1.72)	<.001 (<.001)	.002	<.001	.006
Refractive error (sound eye), D§								
<1.00	67 (16)	13 (8)	42 (27)	12 (12)				
1.00 to <2.00	99 (24)	27 (17)	56 (37)	16 (16)				
2.00 to <3.00	71 (17)	25 (16)	25 (16)	21 (21)				
3.00 to <4.00	61 (15)	25 (16)	12 (8)	24 (24)				
≥4,00	111 (27)	66 (42)	18 (12)	27 (27)				
Mean (SD), logMAR units	2.83 (2.01)	3.54 (2.08)	1.95 (1.67)	3.05 (1.91)	<.001 (<.001)	<.001	.06	<.001
Anisometropia, D§								
<0.50	110 (27)	98 (63)	8 (5)	4 (4)				
0.50 to <1.00	69 (16)	58 (37)	10 (7)	1 (1)				
1.00 to <2.00	65 (16)	...	22 (14)	43 (43)				
2.00 to <3.00	70 (17)	...	43 (28)	27 (27)				
3.00 to <4.00	51 (12)	...	39 (25)	12 (12)				
≥4,00	44 (11)	...	31 (20)	13 (13)				
Mean (SD), logMAR units	1.73 (1.62)	0.30 (0.30)	2.79 (1.52)	2.33 (1.36)	<.001 (<.001)	...	...	.02

*Data are presented as number (percentage) unless otherwise indicated. D indicates diopters; ellipses, not applicable.
†Unadjusted Pvalues from analysis of variance; adjusted Pvalues from analysis of covariance were adjusted tor age as a continuous variable.
‡Unadjusted Pvalues from *ttest.*
§Expressed as spherical equivalent.

Table 3. Baseline Characteristics According to Age at Enrollment*

	Age, y				P†
	<4 (n = 67)	4 to <5 (n = 83)	5 to <6 (n = 135)	6 to <7 (n = 124)	Unadjusted (Adjusted for Cause)
Cause of amblyopia					
Strabismus	35 (52)	30 (36)	40 (30)	51 (41)	
Anisometropia	16 (24)	31 (37)	56 (41)	50 (40)	.03
Combined-mechanism	16 (24)	22 (27)	39 (29)	23 (19)	
Visual acuity (amblyopic eye)					
20/100	27 (40)	18 (22)	27 (20)	23 (19)	
20/80	17 (25)	22 (27)	34 (25)	22 (18)	
20/60	10 (15)	20 (24)	30 (22)	31 (25)	
20/50	5 (7)	15 (18)	31 (23)	33 (27)	
20/40	8 (12)	8 (10)	13 (10)	15 (12)	
Mean (SD), logMAR units	0.57 (0.14)	0.53 (0.13)	0.52 (0.13)	0.50 (0.13)	.005 (.002)
Visual acuity, (sound eye)					
20/40	19 (28)	4 (5)	7 (5)	8 (6)	
20/30	14 (21)	25 (30)	32 (24)	10 (8)	
20/25	12 (18)	27 (33)	38 (28)	36 (29)	
20/20	21 (31)	23 (28)	50 (37)	54 (44)	
20/15	1 (1)	4 (5)	8 (6)	16 (13)	
Mean (SD), logMAR units	0.14 (0.12)	0.10 (0.10)	0.09 (0.10)	0.05 (0.10)	<.001 (<.001)
Intereye difference, lines					
3	22 (33)	27 (33)	44 (33)	35 (28)	
4	23 (34)	26 (31)	34 (25)	34 (27)	
5	7 (10)	15 (18)	31 (23)	25 (20)	
6	9 (13)	9 (11)	15 (11)	18 (15)	
7	6 (9)	5 (6)	10 (7)	9 (7)	
8	0	1 (1)	1 (0.7)	3 (2)	
Mean (SD)	4.3 (1.3)	4.3 (1.3)	4.4 (1.3)	4.5 (1.4)	.59 (.18)
Refractive error (amblyopic eye), D‡					
<1.00	1 (1)	3 (4)	3 (2)	12 (10)	
1.00 to <2.00	3 (4)	6 (7)	6 (4)	18 (15)	
2.00 to <3.00	7 (10)	11 (13)	12 (9)	7 (6)	
3.00 to <4.00	9 (13)	16 (19)	22 (16)	13 (10)	
≥4.00	47 (70)	47 (57)	92 (68)	74 (60)	
Mean (SD), logMAR units	4.75 (1.75)	4.38 (2.17)	4.78 (1.94)	4.21 (2.33)	.11 (.06)
Refractive error (sound eye), D‡					
<1.00	6 (9)	12 (14)	22 (16)	27 (22)	
1.00 to <2.00	13 (19)	19 (23)	34 (25)	33 (27)	
2.00 to <3.00	10 (15)	16 (19)	22 (16)	23 (19)	
3.00 to <4.00	16 (24)	13 (16)	24 (18)	8 (6)	
≥4.00	22 (33)	23 (28)	33 (24)	33 (27)	
Mean (SD), logMAR units	3.27 (1.72)	2.88 (2.08)	2.80 (2.08)	2.58 (2.03)	.16 (.07)
Anisometropia, D‡					
<0.50	18 (27)	26 (31)	27 (20)	39 (31)	
0.50 to <1.00	19 (28)	10 (12)	20 (15)	20 (16)	
1.00 to <2.00	7 (10)	15 (18)	27 (20)	16 (13)	
2.00 to <3.00	11 (16)	17 (20)	26 (19)	16 (13)	
3.00 to <4.00	6 (9)	10 (12)	15 (11)	20 (16)	
≥4.00	6 (9)	5 (6)	20 (15)	13 (10)	
Mean (SD), logMAR units	1.49 (1.51)	1.53 (1.48)	2.01 (1.74)	1.68 (1.61)	.07 (.96)

*Data are presented as number (percentage) unless otherwise indicated. D indicates diopters.

†Unadjusted P value for association between cause of amblyopia and age from x^2 test. All other unadjusted P values were determined using analysis of variance; adjusted P values from analysis of covariance were adjusted for cause of amblyopia.

‡Expressed as spherical equivalent.

included pediatric ophthalmologists and optometrists from both university and community-based practices. The study was designed to approximate clinical practice as much as possible, with the exceptions being the use of randomization to determine the treatment prescribed for each patient and the use of a standardized single-surround HOTV

Table 4. Number of Hours of Daily Patching Prescribed at Enrollment for Patients in the Patching Group According to Baseline Visual Acuity in the Amblyopic Eye*

Hours of Patching	All Patients	Grouped by Visual Acuity in the Amblyopic Eye				
		20/40	20/50	20/60	20/80	20/100
	N =212	n = 19	n = 46	n = 56	n = 42	n = 49
6	92 (43)	12 (63)	22 (48)	27 (48)	19 (45)	12 (24)
8	62 (29)	7 (37)	15 (33)	19 (34)	7 (17)	14 (29)
10	15 (7)	0	1 (2)	0	4 (10)	10 (20)
12	7 (3)	0	1 (2)	2 (4)	2 (5)	2 (4)
Full-time	36 (17)	0	7 (15)	8 (14)	10 (24)	11 (22)

*Data are presented as number (percentage). The number of patching hours was prescribed according to investigator discretion (with a minimum of 6 hours per day); full-time was defined as all or all but 1 waking hours. P = .003 for association between hours of patching and amblyopic eye visual acuity from the Kruskal-Wallis test.

optotype visual acuity testing protocol, which we developed specifically for this study.[7]

The clinical profile of the cohort must be viewed in the context of the eligibility and exclusion criteria for the study (Table 1). The eligibility criteria for enrollment were broad, with the intention to include most children with amblyopia younger than 7 years who were developmentally able to perform single-surround HOTV optotype visual acuity testing. This effectively set a lower age limit of about 3 years, although 7 children between the ages of 2.5 and 3 years successfully completed visual acuity testing and were enrolled. To avoid including prior treatment failures in the study, children who had received more than 2 months of amblyopia treatment in the prior 2 years were not enrolled. The visual acuity limit for the amblyopic eye was set at 20/100 because atropine is not thought to be an effective treatment for worse acuities.[8,9] Eligibility required a 3-line difference in visual acuity between eyes (1) to assure that a true reduction in acuity was present (a reliability study using our acuity testing protocol found that a 3-line interocular difference was required for reasonable certainty that amblyopia was present[7]), and (2) to have a sufficient depth of amblyopia to assess improvement with treatment.

Our cohort's mean age of 5.3 years and the equal sex distribution are consistent with several previous reports describing populations with amblyopia.[5,6,10,11] Our cohort was 83% white, with small percentages of African American, Hispanic, and Asian patients. This racial distribution likely reflects the nature of the investigators' clinical practices. Because our study is not population based, our data should not be used to suggest any demographic variation in the prevalence of amblyopia between ethnic or racial groups.

Our cohort had approximately equal proportions of patients with amblyopia due to strabismus and anisometropia, with about a quarter of the patients having elements of both. The mean ages at enrollment for these groups of children were 5.1, 5.4, and 5.2 years, respectively. These data differ somewhat from those in the population-based study by Woodruff et al[6] of 961 children with amblyopia in the United Kingdom. The authors found the cause to be strabismus in 57%, anisometropia in 17%, and a combination of the two in 27% of patients. The mean ages of children with strabismic, anisometropic, and combination amblyopia were 3.3, 5.6, and 4.4 years, respectively. Our data also differ from those of Shaw et al,[5] who reported that in 1531 children with amblyopia in the United Kingdom, strabismus was the cause in 45%, anisometropia in 17%, a combination of the two in 35%, and deprivation due to cataract or corneal scarring in 3%. In the study by Shaw and colleagues, the median ages of children with strabismic, anisometropic, and combination amblyopia were 3.6, 6.3, and 4.7 years, respectively.

The 2 studies from the United Kingdom differ from ours in 4 important ways. First, extensive prior treatment was an exclusion in our study. This criterion would reduce the proportion of patients diagnosed (and presumably treated) at younger ages entering the ATSl. These younger patients would more often have strabismus, as seen in the 2 studies from the United Kingdom.[5,6] The second difference was our requirement for the children to complete a single-surround HOTV optotype visual acuity testing protocol. This reduced the proportion of patients with strabismus in our cohort by excluding most children with amblyopia younger than 3 years. The third difference was our exclusion of deep amblyopia, also more frequently associated with strabismus.[12,13] Finally, the studies from the United Kingdom defined anisometropia as at least 1 D, compared with the 0.5-D minimum used in the ATSl. However, this creates only a small difference between studies; our cohort included just 18 patients with anisometropia of less than 1 D, and 12 of the 18 had a difference in astigmatism between eyes of+ 1.50 Dor more.

We found that the visual acuity of the amblyopic eyes was similar whether the amblyopia was caused by strabismus, anisometropia, or both conditions. Rodier et al[14] also found no difference in initial acuity among their patients with these 3 types of amblyopia. Although previous studies have suggested that strabismic and combined-mechanism amblyopia represent a more severe physiological deficit, due to active cortical suppression, than purely anisometropic amblyopia,[2,15,16] the restriction of our cohort to children with an amblyopic eye acuity of 20/100 or better limits our ability to address this issue.

As expected, visual acuity in the sound eye was slightly better with older age. This phenomenon may reflect the child's increasing sophistication with testing and optotypes at older ages.[17] For this reason, the interocular difference in acuity should be a useful measure to account for this age effect on acuity testing. However, for assessing change in visual acuity with treatment during

The Pediatric Eye Disease Investigator Group

Writing Committee

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a several-month period (in which the age effect is expected to be minimal), the change in interocular acuity difference may be less useful than the change in amblyopic eye acuity alone; the former is affected by the testing variability in both eyes, whereas the latter is affected by the variability in only one eye.[7,8]

We were surprised by the variation in visual acuity of the sound eye according to cause of amblyopia, which persisted even after statistically adjusting for age, refractive error in the sound eye, and prior treatment for amblyopia. We do not have a simple explanation for why sound eye acuity would be best in patients with anisometropia, worst in patients with strabismus, and intermediate in patients with both anisometropia and strabismus. Levi and Klein[19] previously reported a similar finding for Vernier acuity. They noted that the sound eyes of patients with strabismus had poorer visual acuity than those of patients with anisometropia. The authors suggested that strabismus may produce cortical deficits in the sound eye due to abnormal binocular interactions.

Patching therapy has been the mainstay of amblyopia treatment in North America despite the lack of meaningful data demonstrating its superiority compared with other modalities.[20,21] In planning this study, when we surveyed the Pediatric Eye Disease Investigator Group about their treatment practices for moderate amblyopia, we found that very few prescribed atropine as a primary treatment modality; when patching was prescribed, the intensity of treatment varied widely, from a few hours a day to all waking hours. Our study data support the survey results. The small number of study patients who had been previously treated with atropine compared with the number previously treated with patching is suggestive of the investigators' limited use of atropine as a treatment for amblyopia prior to this study. The number of patching hours prescribed at enrollment for the patching group varied from the allowable minimum of 6 hours per day, prescribed for 43%, to full-time patching, prescribed for 17%. The number of patching hours was related to the severity of the amblyopia but not to the age of the patient or to whether the investigator was institutionally or community based. The optometrist investigators tended to prescribe fewer hours of initial patching than the ophthalmologist investigators.

In summary, we describe the clinical profile of a large cohort of children younger than 7 years with moderate strabismic and anisometropic amblyopia. There was a nearly equal distribution of cause between strabismus and anisometropia (38%), with about 25% of patients having characteristics of both conditions. Although visual acuity in the amblyopic eye did not differ according to cause of amblyopia, acuity in the sound eye was worse with strabismic amblyopia than with anisometropic amblyopia. There was considerable variation in treatment practices with regard to the number of hours of initial patching prescribed by the investigators. However, we did find that the number of patching hours was positively related to the depth of the amblyopia and was greater for ophthalmologists than for optometrists. The data reported in this article define the clinical profile of the patients enrolled in the ATSl. These data will be useful for interpreting the results of the randomized trial comparing patching with atropine as treatments for moderate amblyopia.

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