Comparative Efficacy of Penalization Methods in Moderate to Mild Amblyopia

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• PURPOSE: To compare the efficacy and sensory outcome of pharmacologic and optical penalization in the treatment of moderate to mild amblyopia.
• DESIGN: Randomized clinical trial.
• METHODS: In an institutional setting, two- to 10-year-old children with strabismic or anisometropic amblyopia (visual acuity in the amblyopic eye at least 20/60) who were cooperative to measure visual acuity using the logarithm of the minimum angle of resolution (logMAR) crowded Glasgow acuity cards were randomized into two groups of therapy (n = 35 in each group), 1% atropine, and optical penalization with positive lenses, after stratification by cause of amblyopia. Visual acuity was tested by the logMAR crowded Glasgow acuity cards, after retinoscopic refraction, and deviation angle were measured by the simultaneous prism and cover or Krimsky test. Stereoacuity was determined using the Titmus fly test and Randot preschool or Randot circles stereoacuity test. Change in visual acuity of the amblyopic eye and in interocular difference of visual acuity after six months of amblyopia therapy was the main outcome measure; stereoacuity at six months of therapy was a secondary outcome measure.
• RESULTS: Thirty-one and 32 children completed the outcome examination in the atropine and optical penalization group, respectively. Average improvement in visual acuity of the amblyopic eye was larger in the atropine than in the optical penalization group (3.4 and 1.8 logMAR lines, respectively), as well as average improvement in interocular difference of visual acuity (2.8 and 1.3 logMAR lines, respectively). Better stereoacuity, but nonsignificantly different, was detected in the atropine group.
• CONCLUSIONS: Atropine penalization may be considered more effective than optical penalization with positive lenses. (Am J Ophthalmol 2008;145:562–569.

PENALIZATION, DEFINED AS BLURRING OF THE SOUND eye to force fixation with the amblyopic eye, is used as an alternative to patching in the treatment of amblyopia. Although some specialists believe in the superiority of occlusion therapy,[1] pharmacologic penalization using atropine has been reported to be as effective as patching, at least in moderate amblyopia.[2,3] A potential advantage of atropine could be the sensory outcome, because binocularity is not disrupted, whereas patching during the sensitive period disrupts the neural substrate of binocularity,[4–7] but differences in sensory outcomes have not been found.[2,3] Optical penalization also is used by practitioners in the treatment of amblyopia.[1,8–12] Binocular vision also may be maintained in this therapeutic method, depending on the type of blurring.

Optical penalization has generally been indicated in mild to moderate amblyopia, particularly in children wearing bifocals, and although side effects have not been reported, the possibility of peeking over the glasses is a concern.[11,12] Some clinicians argue that atropine use is effective mainly in hypermetropic patients.[1,10,11] Allergy, toxicity, intolerance, systemic effects, and risk of reverse amblyopia are limitations to atropine use.[2,3,11,13,14] However, it is our clinical impression that the efficacy of optical penalization is lower than that of atropine, and potential sensory outcomes also could be of worse quality in the former, because a focused image may not be present in the two eyes at the same time. In studies reporting the efficacy of both optical and pharmacologic penalization, there is a trend toward better results using atropine,[8,9] but no controlled studies have compared optical and pharmacologic penalization. In the present study, we have compared the efficacy and sensory results of optical and atropine penalization in the treatment of moderate and mild amblyopia in children who were able to cooperate in the measurement of visual acuity using the logarithm of the minimum angle of resolution (logMAR) crowded Glasgow acuity cards test.

METHODS

• PATIENT SELECTION AND SAMPLE SIZE: Subjects included were selected from among children treated for amblyopia between January 2004 and December 2005 in Hospital Ramón y Cajal. The upper age limit for inclusion in the study was 10 years. The lower age limit was determined by the ability to cooperate with visual acuity testing using the logMAR crowded Glasgow acuity cards. For inclusion, interocular difference in visual acuity was at least two logMAR lines (0.2 logMAR units), and visual acuity in the amblyopic eye was at least 0.5 logMAR

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(Snellen equivalent, 20/63), because penalization therapy usually has been recommended in moderate or mild amblyopia.[1–3,8–12] Children who had been treated for amblyopia previously were excluded. Children with organic ocular disease, preceding ocular surgery or botulinum treatment also were excluded.

Anisometropic amblyopia was diagnosed when the spherical equivalent difference was 1 diopter (D) or more or the difference in astigmatism in any meridian 1.50 D or more with no measurable heterotropia. Strabismic amblyopia was defined as heterotropia at distance or near and intereye refractive difference smaller than in anisometropic amblyopia. Children with mixed strabismic and anisometropic amblyopia, defined as heterotropia and intereye refractive difference of at least the magnitude expressed above, were not included—although such patients were encountered frequently—to avoid interaction of two factors in the same subject.

For a 0.1-logMAR units difference between the two groups in change in visual acuity of the amblyopic eye, a standard deviation of 0.15, and a type I error of 5%, a sample size of 35 children in each group yielded 98% power (Power Analysis Statistical System, NCSS, Kaysville, Utah, USA). Participants were randomized to atropine or optical defocus, after stratification into two groups according to cause of amblyopia using a computer-generated sequence of random numbers, by the steering committee.

• **CLINICAL EVALUATION AND TREATMENT PROTOCOL:** Visual acuity was tested using the logMAR crowded Glasgow acuity cards. We used a flip card format with four letters in each size surrounded by a box (Keeler Instruments, Inc, Broomall, Pennsylvania, USA) presented at 3 m. The child was instructed to say the letter or to show the letter on a key card that was the same as the one the examiner was pointing to. Each line contains four letters and the letter size decreases in logarithmic progression. Testing started at 1 logMAR unit (6/60 equivalent). To determine threshold, a level was considered passed when at least three of four letters were identified correctly. When the initial level was passed, the next smallest logMAR level was tested and continued until a level was failed. If the initial level was failed, the next largest logMAR level was tested until a level was passed. To minimize learning effect, the set contains three test charts so that children are not able to memorize letter order, and the eye order of testing was at random. Using this methodology, we tested children between two and 10 years of age. Observers who measured visual acuity were masked to the treatment group. They reported success of blinding in 90.6% (29/32) of the optical and 87% (27/31) of the pharmacologic penalization groups.

We measured eye deviation by the simultaneous prism and cover test or Krimsky test. Refraction was obtained by retinoscopy, 30 to 45 minutes after instilling two drops of 1% cyclopentolate. Stereoacuity was determined by the Titmus fly test and Randot preschool or Randot circles stereoacuity test (Stereo Optical Co, Chicago, Illinois, USA). Follow-up was scheduled with intervals of two to six months, depending on the severity of amblyopia and response to treatment,[11] but for statistical analysis, we recorded data only at the three- and six-month follow-up examinations, which were always required.

During the six-month period of the study, we prescribed 1% atropine (Colircusi Atropina 1%; AlconCusi, Barcelona, Spain) twice weekly when interocular acuity difference was present, and once weekly for maintenance therapy (equal visual acuity in both eyes) until the next follow-up visit. Atropine was withdrawn when visual acuity remained equal in the amblyopic and sound eye on two consecutive follow-up visits, but monitoring without treatment continued. Although daily and weekend treatment with atropine are considered equally effective for the treatment of moderate amblyopia,[15] we used a two-days-per-week schedule to avoid loss of efficacy when one drop was not instilled. Atropine was discontinued when allergy or intolerance occurred and when reverse amblyopia was suspected. Sunglasses were used at the discretion of the child and family. Atropine usually was interrupted within one week before the follow-up examination to maintain some cycloplegic effect and the ability to monitor compliance by dynamic retinoscopy.

Optical penalization was achieved by positive defocus of the sound eye (overplus glass). Using a vectographic projector showing the 20/50 letter at a distance where the amblyopic eye could read it, the patient wore Polaroid glasses over best correction in a trial frame. Sphere was added to the sound eye until the patient could read only letters seen by the amblyopic eye. We used the minimal amount of defocus necessary, checked by fixation switch to the amblyopic eye at distance using this control (in children with strabismic deviation, vectographic control was not necessary).[16] The average positive defocus we used was 1.53 D. Optical penalization was checked carefully and was readjusted if necessary in every follow-up visit. Defocus was discontinued when visual acuity remained equal in the amblyopic and sound eye for two consecutive visits, and visual acuity continued to be monitored.

We evaluated compliance of pharmacologic penalization by dynamic retinoscopy. In the optical penalization group, peeking was observed by examiners during deviation angle measurements and by parents of children at home as compliance assessment. They subsequently reported this behavior in the follow-up visits.

We repeated refraction when decreased visual acuity compared with that of the last follow-up visit was detected, and at the end of the study period. As a general rule, glasses were prescribed for myopia of −2.25 D or higher, hyperopia of 2.00 D or higher, and astigmatism of 1.50 D or higher. Correction of lower degrees of refractive error was used when required to yield the best-corrected visual acuity.

TABLE 1. Characteristics of Amblyopic Children at Enrollment

	Atropine Penalization		Optical Penalization	
	Children Recruited (n = 35)	Children Completing Study (n = 31)	Children Recruited (n = 35)	Children Completing Study (n = 32)
Age (yrs)				
≥2 to <4	8	7	6	6
≥4 to <6	12	12	10	9
≥6 to <8	8	7	10	9
≥8 to <10	7	5	9	8
Mean (SD)	5.8 (2.12)	5.64 (2.16)	6.25 (2.11)	6.11 (2.09)
Iris color				
Brown	18	16	17	16
Green	7	6	6	6
Blue	10	9	12	10
Visual acuity of the amblyopic eye at distance (logMAR)*				
0.5 (0.3)	11	10	9	9
0.4 (0.4)	10	9	9	8
0.3 (0.5)	8	6	10	9
0.2 (0.63)	6	6	7	6
Mean (SD) logMAR	0.41 (0.12)	0.43 (0.12)	0.44 (0.11)	0.44 (0.11)
Mean Snellen	0.38	0.37	0.36	0.36
Interocular difference of visual acuity (logMAR lines)				
2	7	6	8	7
3	10	8	11	11
4	8	8	7	6
5	10	9	9	8
Mean (SD)	3.5 (1.10)	3.64 (1.11)	3.4 (1.0)	3.46 (1.10)
Refraction (diopters)				
Amblyopic eye				
<0.50	5	5	6	4
≥0.50 to <2.00	7	6	6	6
≥2.00 to <3.50	10	9	12	12
≥3.50 to <5.00	9	7	8	7
≥5.00	4	4	3	3
Mean (SD)	2.6 (2.07)	2.53 (1.98)	2.5 (2.10)	2.62 (2.11)
Sound eye				
<0.50	10	9	11	9
≥0.50 to <2.00	9	8	8	8
≥2.00 to <3.50	7	6	5	5
≥3.50 to <5.00	7	6	7	6
≥5.00	2	2	4	4
Mean (SD)	1.79 (2.22)	1.74 (2.2)	1.92 (2.50)	1.94 (2.44)
Stereoacuity (seconds of arc)†				
<800	13	12	12	11
≥800 to <400	7	7	4	4
≥400 to <200	8	6	9	8
≥200 to <100	5	4	6	5
≥100 to <60	2	2	3	3
≥60	0	0	1	1
Mean (SD)	586 (357.54)	564 (349.21)	522.8 (377.27)	520.7 (369.42)
Median	600	600	300	300
Cause of amblyopia				
Anisometropia	17	15	17	15
Strabismus	18	16	18	17

TABLE 1. Continued

	Atropine Penalization		Optical Penalization	
	Children Recruited (n = 35)	Children Completing Study (n = 31)	Children Recruited (n = 35)	Children Completing Study (n = 32)
Deviation angle				
<20 PD	3	3	7	6
≥20 to <30 PD	6	5	4	4
≥30 to <40 PD	5	4	4	4
≥40 PD	4	4	3	3
Mean (SD) degrees	17.06 (5.76)	17.21 (5.63)	15.10 (6.27)	15.09 (6.11)

logMAR = logarithm of the minimum angle of resolution; PD = prism diopters; SD = standard deviation.

*Values in parentheses indicate Snellen equivalent (decimal expression).

†Statistical calculations were made after transforming to log seconds of arc; at the end of the process, values were converted again to seconds of arc for a more friendly format.

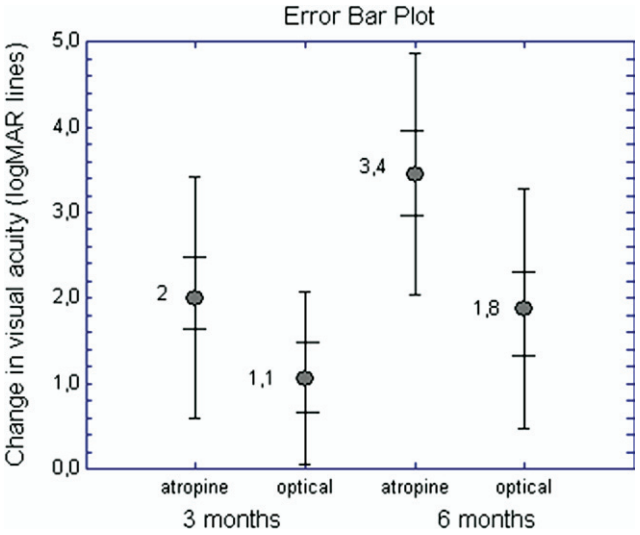

FIGURE. Error bar chart showing mean change in visual acuity of the amblyopic eye (logarithm of the minimum angle of resolution [logMAR] lines) at three and six months from baseline. Circles designate the mean, long bars indicate 95% confidence intervals, and short bars indicate standard deviation.

• STATISTICAL PROCEDURES: The main outcome measure was change in visual acuity of the amblyopic eye. The change of interocular difference in visual acuity was also evaluated. The treatment groups were compared using the unpaired Student *t* test and multiple regression analysis. An analysis of covariance was incorporated to adjust for baseline variables that could be responsible for confounding or interaction. A secondary outcome measure was sensory status at the end of treatment as determined by stereoacuity measurements, compared using the Mann–Whitney *U* test. For statistical comparison of stereoacuity, seconds of arc values were transformed to log seconds of arc, and thereafter converted to seconds of arc again, which constitutes a more friendly format to the reader. For statistical analysis, we used NCSS software (NCSS, Kaysville, Utah, USA).

RESULTS

THE CHARACTERISTICS OF CHILDREN INCLUDED IN THE study are summarized in Table 1. The outcome examination was completed by 32 children (91.4%) in the optical penalization group and by 31 children in the atropine group (88.5%). In the optical penalization group, three children were lost to follow-up. In the atropine group, two patients discontinued treatment because of intolerance, one was withdrawn because the amblyopic eye was treated mistakenly with atropine (subsequently treated with occlusion of the fellow eye), and one was lost to follow-up. Because an association was not found between the treatment group and baseline visual acuity ($P = .2$), refraction ($P = .51$), age ($P = .19$), and gender ($P = .68$), these variables were not considered as confounders.

The average improvement of visual acuity in the amblyopic eye (see Figure) at six months was larger ($P < .01$) in the atropine group (3.4 lines) than in the optical penalization group (1.8 lines). At the three-month examination, improvement was also higher ($P = .02$) in the atropine-treated group (two lines) than in the optical defocus-treated group (1.1 lines). At six months, 80.6% (25/31) of children treated with atropine and only 25% (8/32) of those treated with optical penalization had gained three lines or more of visual acuity in the amblyopic eye. The mean interocular difference in visual acuity also improved more ($P = .03$)—by decreasing—in the atropine group (2.8 lines) than in the optical penalization group (1.3 lines) after six months of treatment. After three months of treatment, improvements were, respectively, of 1.8 lines and 0.9 lines; that is, better results were obtained in the pharmacologic

TABLE 2. Visual Acuity of Children Treated for Amblyopia at the End of the Study

	Atropine Penalization (n = 31)	Optical Penalization (n = 32)
Amblyopic eye (logMAR)*		
≥0.5 (0.3) to <0.4 (0.4)	2	4
≥0.4 (0.4) to <0.3 (0.5)	2	6
≥0.3 (0.5) to <0.2 (0.63)	4	4
≥0.2 (0.63) to <0.1 (0.8)	11	9
≥0.1 (0.8)	12	9
Mean (SD) logMAR	0.07 (0.18)	0.21 (0.20)
Change from baseline (logMAR lines)		
0	1	5
1	3	9
2	2	10
3	9	3
4	7	3
5	9	2
Mean (SD)	3.4 (1.4)	0.18 (0.14)
Sound eye (logMAR)*		
≥0.3 (0.5) to <0.2 (0.63)	1	2
≥0.2 (0.63) to <0.1 (0.8)	3	3
≥0.1 (0.8)	27	27
Mean (SD) logMAR	0.01 (0.10)	0.02 (0.13)
Change from baseline (logMAR lines)		
−1	1	0
0	8	20
1	9	7
2	3	5
Mean (SD)	0.4 (0.7)	0.5 (0.7)
Interocular difference (logMAR lines)		
0	16	5
1	9	7
2	4	13
3	1	4
4	1	3
5	0	0
Mean (SD)	0.7 (1)	1.9 (1.1)
Net change from baseline (%)		
100	16	5
80	1	0
75	4	1
66	3	4
60	0	2
50	2	5
40	1	4
33	1	4
20	2	2
0	1	5
Mean (SD)	79.7 (26.19)	48.15 (31.15)

logMAR = logarithm of the minimum angle of resolution; SD = standard deviation.
*Values in parentheses indicate Snellen equivalent (decimal expression).

penalization group ($P = .04$). The sensory outcome was similar in the two treatment groups, with a mean stereoacuity of 403 seconds of arc in the atropine group and 447 seconds of arc in the optical penalization group ($P = .27$) at six months. Influence and mutual interaction of baseline variables on improvement in visual acuity was discarded by covariance analysis, which demonstrated a significant difference between the two

TABLE 3. Stereoacuity* of Children Treated for Amblyopia at the End of the Study

	Atropine Penalization (n = 31)	Optical Penalization (n = 32)
Stereoacuity		
<800	9	12
≥800 to <400	9	8
≥400 to <200	6	5
≥200 to <100	3	3
≥100 to <60	2	3
≥60	2	1
Mean (SD)	403.22 (285.19)	447.5 (300.22)
Median	400	400
Net change from baseline (%)		
80	1	0
60	2	1
50	5	2
40	5	2
33	7	10
20	8	9
0	3	7
Mean (SD)	33.5 (18.22)	23.43 (16.78)

SD = standard deviation.

*Seconds of arc (statistical calculations were made after transforming to log seconds of arc; at the end of the process, values were converted again to seconds of arc for a more friendly format).

treatment groups ($P < .01$) after controlling for baseline interocular acuity difference ($P = .33$), refraction ($P = .67$), age ($P = .46$), gender ($P = .54$), and iris color ($P = .22$). Visual acuity and stereoacuity measurements obtained at the end of the study are displayed in Tables 2 and 3, respectively.

In the two subgroups of amblyopia considered separately, the result was similar to the overall result at the end of the study. Atropine treatment produced greater improvement in visual acuity of the amblyopic eye than optical penalization both in those with strabismus (3.3 vs 1.7 lines; $P = .02$) and those with anisometropic amblyopia (3.5 vs 1.9 lines; $P = .02$). Stereoacuity outcome was similar for the two treatment groups regardless of the type of amblyopia (498 seconds of arc vs 472 seconds of arc in the strabismus group; $P = .4$; 455 seconds of arc vs 432 seconds of arc in the anisometropic group; $P = .3$). The response to treatment assignment at six months was better, but not significantly different, in children younger than eight years of age than in those aged eight years or older in the atropine group (4.2 vs 2.6 lines; $P = .07$) and in the optical defocus group (2.3 vs 1.6 lines; $P = .09$).

Four myopic children completed the study in the atropine group and three completed the study in the optical penalization group. The range of spherical equivalent refraction was −3.75 to −1.25 D (right eye) and −4.25 to −1.00 D (left eye) in the atropine group and −4.50 to −0.75 D (right eye) and −3.75 to −1.75 (left eye) in the optical penalization group (with two anisometropic patients in the atropine group and one in the optical penalization group). Improvement in visual acuity of the amblyopic eye at six months ranged between one and two logMAR lines in children with pharmacologic penalization, and between one and three logMAR lines in those with optical penalization. Therefore, in this subset of patients, there was no apparent difference in treatment effect between the two methods of therapy (or even optical penalization may be more effective), but we could not draw definite conclusions because of the small number of patients.

Reverse amblyopia was detected in one child in the atropine group after 15 weeks of treatment, that is, in 3.22% of the children in this group (1/31). Therapy was discontinued and visual acuity remained at 20/25 Snellen in both eyes at the end of the study period. No cases of reverse amblyopia were detected in the optical penalization group. Noncompliance was suspected by reported peeking and behavior in five of the 32 children in the optical penalization group (15.62%) and by dynamic retinoscopy findings (ability to accommodate) in four of the 31 children in the atropine group (12.9%).

DISCUSSION

PHARMACOLOGIC PENALIZATION WITH ATROPINE MAY be considered more effective than optical penalization by wearing a plus defocus lens in the treatment of moderate or mild amblyopia. Although using optical penalization is helpful in treating amblyopia, the effect of this treatment after six months (1.8 lines) is only slightly larger than half the effect of atropine penalization (3.4 lines). The stronger effect of atropine may be explained in part by the better compliance in comparison with optical penalization (probably related to maintenance of good distance visual acuity in the amblyopic eye), inability to circumvent its cycloplegic effect, and prolonged tolerable induced loss of high spatial frequency detection at near. It could be argued that treatment dose is tailored to the individual patient's acuity deficit in the optical penalization group but not in the atropine group. The reason for this protocol is that daily and weekend atropine are equally effective for the treatment of moderate amblyopia[15] (using it twice a week prevents accommodation and consequently vision at near all the time), and fixation switch is not absolutely necessary for atropine to be effective,[15] whereas we must be sure that the patient uses the amblyopic eye at distance with the minimal amount of optical penalization for efficacy and increase of patient acceptance.[16]

TABLE 4. Summary of Recent Studies on Penalization for the Treatment of Amblyopia

	Atropine Penalization			Optical Penalization		
	Lines of Visual Acuity Improvement of Amblyopic Eye (End of Treatment)	Treatment Duration	No.	Lines of Visual Acuity Improvement of Amblyopic Eye (End of Treatment)	Treatment Duration	No.
Repka and Ray, 1993*	~2	13 mos	79	~1.3	29 mos	87
Simons and associates, 1997*	2.7 (F)	1.4 yrs (F)	38 (F)	1.9	2.9 yrs	52
	1.9 (I)	1.1 yrs (I)	73 (I)			
Foley-Nolan and associates, 1997†	~6	7.2 mos	18	NA	NA	NA
PEDIG 2002†	2.84	6 mos	194	NA	NA	NA
PEDIG 2004†	2.3 (D)	4 mos	83	NA	NA	NA
	2.5 (W)	4 mos	85			
Present study†	3.4	6 mos	31	1.8	6 mos	32

D = daily atropine; F = full-time atropine; I = intermittent atropine; mos = months; NA = not applicable; PEDIG = Pediatric Eye Disease Investigator Group; W = weekend atropine.

*Retrospective survey.

†Comparative controlled trial.

The magnitude of improvement in visual acuity at six months is in agreement with the effect of atropine therapy and optical penalization as reported by different studies (Table 4).[2,3,8,9,13,17] These studies report an improvement of two to six lines after between four months and more than one year of atropine treatment.[2,3,9,13,17] Optical penalization was associated with an average improvement of 1.3 to 1.9 lines after more than two years of treatment on average.[8,9] The reasons for the slightly larger improvement we observed in comparison with some of the previously conducted studies may be the lower level of initial amblyopia depth, which may enhance compliance of therapy, and the longer period of treatment or more controlled situation in other cases.

After a loss to follow-up of three cases in one group and four cases in the other group, the power of the study declined to 93%. Loss to follow-up did not cause any apparent bias in the study (neither did initially declining to be included in the treatment groups) because the characteristics of the pretreatment group variables did not vary. We tried to eliminate or identify confounding variables, using selection criteria, stratification, and randomization in the design of the study and using covariance analysis in the analysis process. Confounding or interaction variables could not be identified in the present study. The power of the analysis in the subgroups defined by cause of amblyopia was 78%.

A weakness of this investigation is related to compliance assessment, which, particularly in the optical penalization group, was not addressed easily because of difficulty in reporting frequency of peeking over glasses.

The principle of intent-to-treat or treatment assignment analysis (i.e., patients are included in the analysis of the group to which they were originally assigned, regardless of compliance or any events) has been used so that the study gives information on the effectiveness of the treatments under everyday practice conditions. Also, it preserves baseline comparability of confounders and it maintains the original power of the study samples. The only exception is a boy withdrawn because his amblyopic eye was mistakenly treated with atropine, and he required occlusion therapy. However, when patients under suspicion of unsatisfactory compliance are removed from the analysis, the results are essentially the same as those obtained when included, but with significant loss of power. Therefore, the influence of less compliant patients is not strong enough to cause changes in difference of treatment effect. Another reason to use the intent-to-treat principle is that eliminating patients for statistical analysis based on the lack of compliance could be a source of bias (noncompliant patients may be those with deeper amblyopia).

We did not observe differences in stereoacuity results between the two treatment methods used. When patients wear an overplus glass before the sound eye (positive defocus), the amblyopic eye is used at distance, whereas the penalized eye may be used at near (instead, the amblyopic eye may be used at near as well as at distance). Images of the two eyes are not simultaneously in focus, but may be alternatively (e.g., at near and distance). However, during atropine penalization, the two eyes may be used simultaneously at distance. The relationship between visual acuity and stereoacuity has been reported, by monocular change of visual acuity using fogging or induced anisometropia,[18–23] but this relationship may not be linear.[23] Visual acuity may be normal with no measurable stereopsis or poor with good stereoacuity.[18,20] These findings help explain why difference in visual acuity improvement between the two treatment groups is not paralleled by differences in stereoacuity in the present study.

The present study indicates that pharmacologic penalization with atropine is more effective than optical penal-

ization with positive lenses. Although the latter option may be of use in specific clinical situations (concurrent bifocal prescription, less hyperopic children, and mild amblyopia), we believe that pharmacologic penalization may be considered as first-line penalization therapy for amblyopia.

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