Penalization versus Part-time Occlusion and Binocular Outcome in Treatment of Strabismic Amblyopia

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Objective: The purpose of the study is to compare the visual outcome of occlusion versus penalization treatment of strabismic amblyopia, with particular attention to binocularity outcome.

Design: The study design was a retrospective study.

Participants: Patients with strabismic amblyopia, 75 receiving penalization alone, 87 with a history of occlusion treatment who were later treated by penalization, and 30 treated by means of part-time occlusion (2 to 6 hours/day) participated in this study.

Main Outcome Measures: Logarithm of the minimum angle of resolution (logMAR) visual acuity and binocularity index were measured.

Results: No statistically significant difference was found between outcomes for the penalization groups with and without a history of occlusion, either by univariate analysis or by multivariate analysis controlling for initial-visit age, acuity, and binocularity status. One marginally significant outcome difference was found between the pure penalization and part-time occlusion groups by univariate analysis, but no significant difference was found in the multivariate analyses controlling for the same three variables at the initial visit. All visual outcome differences between the pure penalization and part-time occlusion groups were less than 1 logMAR line visual acuity or less than a half-unit on the binocularity index.

Conclusions: The study provided no evidence of a difference in visual function outcome between penalization and occlusion, in terms of either statistical or clinical significance, although limitations of the patient samples used preclude these data from showing conclusively that there was no such difference. The lack of any other study adequately comparing these two treatment methods, in combination with the current study's demonstration of the difficulty of making adequate retrospective-based comparison despite a large patient base (n = 1413), suggests that a large prospective, randomized comparative treatment trial is needed. If atropine penalization, with its high acceptability to patients and parents, is found to produce results comparable with those of occlusion in cases of mild-to-moderate amblyopia, as the current and previous smaller studies suggest, then reconsideration of the standard of care for such amblyopia cases is indicated. Ophthalmology 1997;104:2156-2160

Amblyopia treatment by means of penalization dates back to at least Worth and occlusion treatment much further. Since penalization traditionally has been viewed as useful only for occlusion treatment failures or for postocclusion acuity maintenance, there have been few studies comparing these two treatment methods. One small (n = 38), retrospective study reported better visual acuity outcomes in a group of children older than 6 years of age treated with atropine penalization than was obtained in a group
of younger children who were occluded, but no statistical comparison was made.\(^9\) (The nominally more neurally plastic younger children might have been expected to produce better results.) Another small \((n = 25)\), comparative study was done prospectively, with randomization and compliance monitoring, and found no difference in visual acuity outcome of the amblyopic eye between the two methods (i.e., penalization was found to be as efficacious as occlusion).\(^1\) A recent prospective study of 36 patients with no history of amblyopia treatment came to the same conclusion, finding no statistically significant difference in outcome between the two forms of treatment.\(^9\)

In view of evidence in animal models that unilateral or alternating occlusion during the binocular sensitive period can cause irreversible disruption of binocularity,\(^2\) binocular prognosis is of particular interest in such a comparison. Evaluation of this issue is complicated by lack of information about the human binocularity sensitive period and about the treatment implications of the already-compromised binocularity of those with amblyopia (see review in preceding article\(^9\)). For instance, human infants with esotropia who undergo occlusion treatment in some cases still have at least gross stereopsis develop, even on random dot stereograms,\(^1,10,11\) and kittens with occlusion-induced deprivation amblyopia have been shown to be able to recover at least contour stereopsis with appropriately scheduled part-time reverse occlusion.\(^12\)

The current study involved retrospective analyses of two patient populations to compare the efficacy of penalization and occlusion, particularly regarding binocular outcome. The first analysis involved a comparison of one group of penalization patients from our previous work\(^9\) who had a history of occlusion treatment with another group who were treated solely by penalization. The second analysis compared the latter group with a group of patients for whom identical clinical measurement data were available and who had been treated by means of part-time occlusion or not.

**Materials and Methods**

Best-corrected visual acuity was measured using linear Snellen optotypes or single or linear Allen figures. Visual acuity was coded as in the previous article,\(^9\) with scaling of partial-line results. As in the previous article, depth of amblyopia was defined as the logarithm of the minimum angle of resolution (logMAR) visual acuity ratio between eyes. Binocular function was tested by the Worth 4-dot test at near and at distance, and stereopsis evaluated with the Titmus stereo fly and Randot Circles stereo tests. For analysis, we once again followed the practice of the previous article,\(^9\) characterizing binocularity with an index ranging from 0 to 4: 0 indicated complete suppression; 1 indicated a moderate central suppression scotoma with peripheral fusion, indicated by fusion on the Worth 4-dot test at near only; 2 indicated a small suppression scotoma and peripheral fusion and/or gross stereopsis, as shown by fusion on the Worth 4-dot test at distance or passing the Titmus stereo fly or both; 3 indicated moderate stereovision (100–400 arc seconds) on the Randot Circles test; and 4 indicated good stereovision (≤70 arc seconds).

**Analysis 1**

A total of 163 patients with strabismic amblyopia were identified in a previous study of penalization who met inclusion criteria of no ocular or neurologic abnormality, at least 1 logMAR line of difference in acuity between eyes at treatment onset, and adequate acuity and binocularity measurements obtained at the treatment onset visit, the end-of-treatment visit, and, for a subset of the patients, at a long-term follow-up visit.\(^7\) Of these 163 patients, 88 had a history of occlusion treatment under various regimens before penalization, whereas 75 patients in that study were treated purely with some form of penalization. Three types of penalization had been used: full-time or intermittent atropine penalization or optical penalization. To determine whether occlusion history was associated with outcome, the patients within each of these groups with a history of occlusion or attempted occlusion treatment were compared with the patients within that group who had been treated purely with penalization with regard to age, depth of amblyopia (defined below), binocularity index (defined below), and anisometropia, all at the initial visit. Outcome variables for the patients falling into the two categories within each group then were compared as well: depth of amblyopia and binocularity index at the end-of-treatment and long-term follow-up visits and the amount of change of the amblyopia and binocularity measures between the initial visit and each of those two visits. Potentially confounding variables accounted for by multivariate methods in this latter analysis were age, depth of amblyopia, and pretreatment binocularity status.

**Analysis 2**

A population of 850 patients with strabismic amblyopia treated by occlusion were identified by chart review. The same diagnostic measurements were available for these patients as for the patients of the previous study used in analysis 1,\(^9\) making adequate comparison possible. As in the case of those three groups, patients with ocular or neurologic abnormality were excluded, as were patients with less than 1 logMAR line of difference in visual acuity between eyes at the initial visit and patients for whom the diagnostic measures were not available for at least the initial- and end-of-treatment visits. A total of 30 patients (3.5%) met these inclusion criteria. An institutional review board-approved protocol was followed to maintain patient confidentiality.

The following data were abstracted for each patient: cycloplegic refraction at the initial visit, age, amblyopia depth, and binocularity index for each of three visits. The three visits were defined as the initial visit (i.e., when treatment was begun), the end of treatment, and again, when available, the final long-term follow-up visit (i.e., the last time patient was seen).

The 30 patients with part-time occlusions were com-
pared regarding status at the initial and end-of-treatment visits, and at the long-term follow-up visit when data were available. They also were compared with 75 patients drawn from all 3 groups in the previous study (full-time atropine, intermittent atropine, optical) who had been treated purely with penalization. In view of the similarities among the three groups in both the previous study\(^7\) and in the analysis 1 results detailed below, the patients with different penalization regimens were treated as a single group in this analysis.

In the statistical analysis, two-tailed \(t\) tests for paired data were used for evaluation of mean change pretreatment to post-treatment, the Kruskal–Wallis test was used for comparing median outcomes among treatment groups, Fisher’s exact test was used to compare proportions between treatment groups, and multivariate relationships were assessed by means of multiple linear or multiple logistic regression.

### Results

#### Analysis 1

With one exception, patients in the full-time atropine, intermittent atropine, and optical penalization groups with a history of occlusion treatment were not found by univariate analysis to differ significantly from the patients in each of those groups, respectively, who had been treated purely by penalization regarding age, depth of amblyopia, binocularity index, or amount of anisometropia at the initial visit, depth of amblyopia, or binocularity index at the later visits. The exception was that in the optical penalization group, patients with a history of occlusion had a marginally, significantly \((P < 0.02)\) larger mean amount of anisometropia than did those treated only by penalization.

We then assessed the effect of history of occlusion on the outcome variables in each of the three treatment groups, adjusting for the potentially confounding variables of age, depth of amblyopia, and binocularity index at the initial visit in a multivariate model. The outcome variables analyzed were amblyopia depth and presence or absence of any degree of binocularity at the end-of-treatment and long-term follow-up visits. Once again, there were no significant differences in outcome between patients in the occlusion and no-occlusion history categories in any of the three penalization treatment groups. In summary, treatment outcome after penalization was not found to differ significantly whether the patients had a history of occlusion or not.

#### Analysis 2

Patients in the part-time occlusion group were treated by regimens varying from 2 to 6 hours of occlusion per day and, in some cases, with a variable number of hours per day over a course of treatment. Results are summarized in Table 1.

All visual outcome differences between the penalization-only and part-time occlusion groups were less than 1 logMAR line acuity or less than a half unit on our binocularity index (Table 1). Univariate and multivariate approaches were used to compare the two groups. The groups were quite similar as to age and visual status at the initial visit (Table 1), with none of the differences being statistically significant. The only statistically significant outcome difference between these two groups by univariate analysis was a borderline significant greater degree of improvement of the visual acuity status (i.e., depth of amblyopia) in the penalization-only group between the initial and long-term follow-up visits (Table 1). Multivariate analysis was made of the outcome variables (i.e., amblyopia depth and presence or absence of binocularity at any level at the end-of-treatment and long-term follow-up visits) in the two treatment groups controlling for age, depth of amblyopia, and binocularity index at the initial visit. No significant differences were found.

### Discussion

The current study found no substantial evidence that penalization treatment of strabismic amblyopia produces different outcome on either monocular (i.e., visual acuity) or binocularity measures than does occlusion treatment. The only exception to this finding was a marginally, statistically significant greater amount of amblyopia reduction found by univariate analysis in the penalization-only than in the part-time occlusion group between the initial and long-term follow-up visits (Table 1). However, this difference was not found in the multivariate analysis controlling for age and visual status at the initial visit. Even the differences found by univariate analysis were so small—less than 1 logMAR line on the amblyopia depth measure and less than a half step on the binocularity index (Table 1)—that they would be considered clinically insignificant.

Our study has several limitations, however, that prevent a definitive conclusion. In analysis 1, in keeping with a difficulty confronting previous studies,\(^9\) patients classified as occlusion treatment failures may in fact have been compliance failures rather than true occlusion treatment failures. (It has been reported anecdotally that patients in whom (full-time) occlusion was carried out correctly showed no further improvement from subsequent penalization, although no explicit data were reported to support this conclusion.\(^9\) To the extent that some of the patients in the current study had not in fact experienced intended occlusion, of course, our analysis does not represent an evaluation of the effects of true occlusion.

In analysis 2, the use of part-time rather than full-time occlusion in the sample of patients with occlusion means that all the patients had more binocular than occluded (monocular) visual experience during the course of treatment. Whether this binocular experience served to maintain binocularity analogous to the binocularity maintained
However, these criteria limited the sample to patients tempted to control for this problem as much as possible. This ensured that the only selection constraint outside of possible limiting characteristics from the practices themselves was the study’s inclusion criteria. However, these criteria limited the sample to patients old enough at their first visit to cooperate with standard clinical testing of visual acuity and binocularity. As reviewed briefly in the previous article,9 this age limitation may have constrained the responsiveness of the visual system to any treatment, because of reduced neural plasticity.

In conclusion, although the current study does not resolve the matter, it adds to previous evidence14 that use of atropine penalization as a primary treatment of mild-to-moderate amblyopia may produce both monocular and binocular results at least comparable to those of traditional occlusion. If so, there may be reason to reconsider whether atropine penalization is a viable alternative to occlusion as the standard of care for amblyopia at those levels or, indeed, whether such penalization may be preferable to occlusion in view of its high acceptability to both patients and parents.49 solving the classic problem of obtaining compliance in occlusion treatment.12 However, adequate re-evaluation of the standard of care will require a large, randomized, prospective study comparing these two techniques.

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References


