LONG TERM STUDY OF ACCOMMODATIVE ESOTROPIA*

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- The authors thank Cynthia Brasseaux and Lisa Curole for their assistance with data collection and entry, and Blandnya Sciove for her assistance in data cleaning. Pamela Getson, PhD, assisted with the early study design and implementation.

ABSTRACT

Purpose: Previous studies of accommodative esotropia have been hampered by bias-prone methods of data collection and analysis, and small sample size.[1-6] The studies have conflicting conclusions, causing uncertain results. This study aims to determine long-term results of standard treatment of accommodative esotropia and identify predictors of outcome, while minimizing bias in data collection and analysis, using the largest possible sample size.

Methods: A research assistant collected data from all files of a large, long-established pediatric ophthalmology practice (MMP). The assistant was given standardized collection forms, which allowed inclusion of all patient data points over all visits. The assistant was masked as to study goals. She was instructed to include any patient with esotropia, who had been prescribed glasses during treatment. Descriptive terms were converted to code numbers. A second, similarly masked research assistant entered data into a computerized database. Criteria for patient inclusion were designed to conform to earlier studies by IHL and MMP, and were implemented by computer.

Results: The database totaled 1307 patients (747,717 data points). Of these, 354 qualified for this analysis. A greater difference between near and distance esodeviation (AC/A relationship) correlated with a higher rate or deterioration of accommodative esotropia control. ($p<.0001$). Deterioration also positively correlated with earlier age of onset, inferior oblique overaction, and amblyopia.

Conclusions: This study agrees with our previous findings that a high AC/A relationship increases the likelihood of deterioration of accommodative esotropia[1], thus confirming the integrity of the database. This unique, unbiased dataset will be used for future analyses of esotropia.

INTRODUCTION

Despite greater than 135 years experience and numerous studies and articles on the subject, the treatment of accommodative esotropia remains controversial. Agreed-upon diagnostic criteria and treatment regimens have yet to be established.

Published studies of accommodative esotropia have usually involved review of patient records by the practicing pediatric ophthalmologist, who then self-analyzed the data[1-8]. This subjected these studies to potential bias at a number of stages. Other studies have attempted a more objective approach by evaluating patients prospectively[9], but they are limited as to length of follow-up possible, and also subject to bias in patient selection and examiner testing.

After successful alignment of a child's eyes with spectacle correction, there remains a risk that the control will deteriorate, requiring surgical correction to maintain alignment. Prior studies by authors IHL and MMP[1,2] were performed to evaluate the hypothesis that a higher rate of deterioration of accommodative esotropia occurred when the difference between the full cycloplegic refraction-corrected distance and near alignment in prism diopters (AC/A relationship) was high. The results showed a statistically significant correlation between deterioration rate and the AC/A relationship, but the study was hampered by small sample size, (119 patients), which precluded testing of subgroups. Additionally, the data was collected by author IHL, who was cognizant of the hypothesis being tested, subjecting the study to potential bias.

A study was designed to fully utilize the data present in the large, long-established pediatric ophthalmology practice (MMP) utilizing methods in data collection and analysis, which would reduce bias to a minimum.

METHODS

A research assistant was hired to collect data from esotropia patients who had been seen in the private pediatric ophthalmology practice of Dr Marshall M Parks. She had no prior ophthalmologic experience, and was not informed about study goals, or the earlier accommodative esotropia research. She was instructed to include all esotropic patients who were prescribed glasses at any time during treatment. The information was entered on specifically designed data collection forms. Descriptive terms were translated to numeric codes. All charts in Dr Parks' files were reviewed, and 1307 were coded.

Dr. Parks' examination and management protocol did not change over the 40 years of clinical practice covered by this study. Ocular alignment was obtained with prism, cover-uncover, and alternate cover measurement with accommodation control at 6 and 0.33 meters. Refractive state was determined by retinoscopy 40 minutes after instilling one drop of 2% cyclopentolate (combined with one drop of 1% tropicamide for darkly pigmented irides) on the anesthetized corneas.

At the LSU Eye Center, another research assistant entered the data into a computerized database. Records were identified by number only, protecting patient confidentiality. The data entry assistant was similarly masked as to study background or plan.

Data was sorted into separate data groups for each analysis by a non-medical computer scientist (SPI), and analyzed using the Statistical Analysis System (SAS Institute, Cary, NC) by a statistician (HWT). Analyses of counts were conducted using an exact method for chi square analysis.[10] Continuous variables with two class levels were analyzed using the t test after checking the assumption of equality of variances and using the appropriate form of the t test.[11] In cases where multiple means were compared, the analysis of variance (ANOVA) was used with post-hoc comparisons conducted after finding a significant overall F test for the ANOVA. The post-hoc comparisons were conducted using the method of simulation-based multiple comparisons.[12]

Analysis for this study was designed to conform to the authors' previously published study on accommodative esotropia. Criteria for inclusion in this study from the database were:

1. Onset of esotropia prior to 8 years of age in a child having otherwise normal eyes.
2. Alignment by spectacles alone to within 8Δ for both distance and near viewing.
    a. (The analysis was then repeated using all the same criteria, but with initial alignment within 4Δ.)
3. Minimum of 5 years follow-up.

Exclusion criteria were:

1. Anisometropia greater than 1.5 D spherical equivalent
2. Amblyopia of 20/100 or greater.
3. Dissociated vertical deviation.
4. Previous extraocular muscle surgery.
5. Absence of follow-up within 2 years after receiving the initial spectacles.
6. Mental retardation.

The AC/A relationship (ratio) is defined according to the difference between the near and distance prism and alternate cover measurements. Less than 10Δ is considered within the range of normal, grade 1 high AC/A is 10-19Δ, grade 2 is 20-29Δ, and grade 3 is 30Δ or greater. The maximal AC/A ratio on the chart reviewed was used to grade the AC/A for each patient.

RESULTS

The database totaled 1307 patients, with 747,717 data points. Of the 1,307 records in the database, 354qualified for this study. Mean follow-up was 10.6 years (range 5-42 years).

Average age of onset was 2.7 years (range 0 to 7.6). Bifocals were prescribed for 170 patients.

The study group was reconfigured using all the same criteria, except the initial successful alignment with spectacles alone was defined as 4Δ or less, rather than the 8Δ or less. The reason for this exercise is related to the criticism of the first study that 8Δ selected as a successful alignment status was excessive(footnote). This reduced the study group size to 335. All tables summarizing the results compare the two criteria.. Either of the two gives a similar trend.

Incidence of deterioration increased significantly with increasing AC/A grade (chi square 27.37, $p < .0001$). (Table 1).

Mean AC/A averaged over all presurgical visits was 13.5 in the deteriorated group, and 8.2 in the undeteriorated ($t=5.1$, $p < .0001$). Mean AC/A averaged over all visits was 10.9 in the deteriorated group and 8.1 in the undeteriorated ($t=3.1$, $p < .002$). (Table2).

As expected, incidence of bifocal use increased with increasing AC/A grade (Table3). Mean hyperopic spherical equivalent, averaged over all visits, was negatively correlated with AC/A grade($p < .0001$), as was the maximal hyperopia recorded over all visits ($p < .0001$). Hyperopia recorded on each initial visit was also negatively correlated with AC/A grade ($p < .0001$). (Table4).

Mean delay-to-treatment (as per parental history) was not significantly different between the deteriorated and undeteriorated groups (Table 5). Incidence of amblyopia was significantly higher in the deteriorated vs. undeteriorated groups (Table 6).

Inferior oblique overaction was strongly correlated with deterioration ($p = .0005$), but inferior oblique overaction at initial examination (Table7) was not significantly higher in the deteriorated groups (Table 8). Mean age of onset was significantly lower in the deteriorated then the undeteriorated groups ($p < .0001$) (Table 9). Time to deterioration was compared by AC/A grade, and did not show significant differences (Table 10).

DISCUSSION

This study agrees with our previous findings that a high AC/A relationship increases the likelihood of deterioration of accommodative esotropia, thus confirming the integrity of the database.[1] The other findings from the earlier study, which are also confirmed here, were the lesser hypermetropia associated with greater AC/A grade and the earlier age of onset in the deteriorated group. The significant associations between amblyopia and deterioration, and maximum inferior oblique overaction and deterioration seen in this study were not demonstrated in our original study. This difference may be explainable by the greater sample size of this database.

Other studies have examined the rate of deterioration of accommodative esotropia as correlated to the AC/A relationship or ratio. Von Noorden[5] found a higher rate of deterioration when the AC/A ratio was low, but his study measured the gradient AC/A

ratio. Another study using gradient AC/A found no correlation to deterioration.[6] The gradient AC/A measures the near alignment response to incremental addition of plus lenses. A child who's excessive near convergence responds poorly to additional plus correction would have a low AC/A ratio by the gradient method, but may have a high distance-near relationship, rendering these studies non-comparable to studies of the distance-near relationship.

Raab reported 13% rate of deterioration in accommodative esotropes with normal AC/A relationships, and a 21% rate in those with high AC/A relationships.[3] The differences were not statistically significant. The smaller sample size of his study, and possibly shorter mean follow-up may account for the lack of statistical significance.

Our finding of increasing hypermetropia with decreasing AC/A grade was reported by other authors.[3,4,12] Also, the increased risk of deterioration with earlier onset of accommodative esotropia, as demonstrated here, is consistent with other reports.[4,6]

Delay-to-treatment was not shown to significantly impact the risk of deterioration, but the study group included only cases which were initially successfully aligned with spectacles alone. Excessive delay would presumably cause early deterioration, prevent initial spectacle alignment, eliminating the case from this study group.

This study analyses a small subset of the larger database of esotropia patients. These results serve the dual purposes of supporting our earlier work and the integrity of this complex database. This database now promises the unique opportunity to study and compare other groups of esotropia patients, and other parameters of all the patients. Our initial impression after trying to group these cases, is that esotropia patients are a more complex and heterogeneous population than is generally appreciated. From this large, long-term practice (MMP), all patients with esotropia and glasses are included in the database, and await study.

The use of unbiased data collection and data entry personnel is unique in this study. Data analysis required defining parameters precisely, and programming the computer to sort the patients into the subgroups. This prevents bias in diagnosis, for example. Prospective following of patients confers no reduction of bias in a study if the examiners are not masked as to study goals or patient status. A clinical trial of an intervention requires diagnosis of a disorder, random assignment of an intervention or control treatment, and prospective, masked following of the patient for a defined period of time.[9] The value of spectacles in treatment of some esotropia patients is not in doubt, but the natural history of these patients over time is subject to speculation. There is disagreement over diagnostic criteria for accommodative esotropia, need for bifocal for high AC/A cases, timing of surgery, etc. The long-term nature of these problems would render a classical clinical trial unfeasible. Although limited, short-term questions, (such as the recent successful trial comparing efficacy of atropine in amblyopia treatment), can be addressed with a clinical trial , the multiple questions still remaining in esotropia treatment would require a long-term cohort study, akin to the Framingham Heart Study.[10] The effort and expense would be prohibitive.

The patients in this database represent all esotropia patients treated with glasses by a single pediatric ophthalmologist in private practice during a period of over 50 years. Each visit is documented on the record, always typed, and presented in a consistent format. Although this database was necessarily collected using retrospective data, methods were employed to minimize bias in data collection and analysis, and the patient care was delivered before this study was envisioned. These factors should reduce bias to the minimum level possible within reasonable limits of time and expense.

TABLES

Numbers indicate study group as initially defined. Numbers in parentheses indicate repeat analysis with study group limited to those with initial spectacle alignment to within 4Δ for both distance and near. Total numbers of patients may differ between tables due to missing values.

TABLE1
Deterioration by AC/A Grade

	Normal	Grade 1	Grade 2	Grade 3	Total
Deteriorated	35 (29)	40 (36)	46 (42)	56 (52)	177 (159)
Undeteriorated	67 (66)	52 (52)	31 (31)	27 (27)	177 (176)
Total	102 (95)	92 (88)	77 (73)	83 (79)	354 (335)

TABLE2
Mean AC/A by Deterioration Status

	Mean AC/A -all visits	Standard deviation	Mean AC/A - presurgical	Standard deviation	number
Deteriorated	10.9 (11.2)	8.5 (8.7)	13.5 (13.8)	11.1 (11.5)	177 (159)
Undeteriorated	8.2 (8.2)	7.9 (7.9)	8.2 (8.2)	7.9 (7.9)	177 (176)

Table 3
Bifocal Use by AC/A Grade
(Near Distance Prism Cover Test)

Bifocal Prescribed	Normal	Grade 1	Grade 2	Grade 3	Total
Yes	4 (4)	39 (36)	72 (67)	74 (72)	188 (179)
No	98 (91)	53 (52)	6 (6)	9 (7)	166 (156)
Total	102 (95)	92 (88)	77 (73)	83 (79)	354 (335)

TABLE 4
Mean Hypermetropia by AC/A Grade
(ANOVA)

	Normal	Grade 1	Grade 2	Grade 3
Mean hyperopia – all visits	3.67 (3.83)	3.25 (3.32)	2.34 (2.32)	2.26 (2.29)
Maximum hyperopia	4.38 (4.54)	4.03 (4.11)	3.21 (3.20)	3.45 (3.49)
Hyperopia – initial visit	3.62 (3.77)	3.05 (3.11)	2.30 (2.29)	2.20 (2.20)

TABLE 5
Delay-to-Treatment

	Mean Delay-to-Treatment (mos)	Standard Deviation	Number
Deteriorated	7.9 (7.5)	13.6 (11.9)	129 (116)
Undeteriorated	7.3 (7.2)	14.3 (12.5)	115 (115)

TABLE 6
Amblyopia vs. Deterioration

	Amblyopia present	Amblyopia absent	Total
Deteriorated	65 (53)	67 (62)	132 (115)
Undeteriorated	42 (41)	89 (89)	131 (130)
Total	107 (94)	156 (151)	

TABLE7
Inferior Oblique Overaction-Initial Visit

	Normal	1+IO	2+IO	3+IO	Total
Deteriorated	149	10	3	0	162
Undeteriorated	149	7	6	2	164
Total	298	17	9	2	326

TABLE 8
Maximum Inferior Oblique Overaction-All Visits

	Normal	1+IO	2+IO	3+IO	Total
Deteriorated	104 (93)	25 (22)	21 (19)	26 (24)	176 (158)
Undeteriorated	139 (138)	11 (11)	15 (15)	11 (11)	176 (175)
Total	243 (231)	36 (33)	36 (34)	37 (35)	352 (333)

TABLE 9
Age of Onset

	Mean Age of Onset	Standard Deviation	Total
Deteriorated	1.9 years (1.9 years)	1.6 (1.38)	151 (137)
Undeteriorated	2.7 years (2.6 years)	1.7 (1.5)	142 (141)

TABLE 10
Time to Deterioration

	Normal	Grade 1	Grade 2	Grade 3
Deteriorated	2.0 years	2.5 years	2.5 years	2.3 years

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