The Development of Myopia Among Children With Intermittent Exotropia

NOHA S. EKDAWI, KEVIN J. NUSZ, NANCY N. DIEHL, AND BRIAN G. MOHNEY

• PURPOSE: **To describe the long-term refractive error changes in children diagnosed with intermittent exotropia (IXT) in a defined population.**

• DESIGN: **Retrospective, population-based observational study.**

• METHODS: **Using the resources of the Rochester Epidemiology Project, the medical records of all children (<19 years) diagnosed with IXT as residents of Olmsted County, Minnesota, from January 1, 1975 through December 31, 1994 were retrospectively reviewed for any change in refractive error over time.**

• RESULTS: **One hundred eighty-four children were diagnosed with IXT during the 20-year study period; 135 (73.4%) had 2 or more refractions separated by a mean of 10 years (range, 1–27 years). The Kaplan-Meier rate of developing myopia in this population was 7.4% by 5 years of age, 46.5% by 10 years, and 91.1% by 20 years. There were 106 patients with 2 or more refractions separated by at least 1 year through 21 years of age, of which 43 underwent surgery and 63 were observed. The annual overall progression was −0.26 diopters (SD ± 0.24) without a statistically significant difference between the observed and surgical groups ($P = .59$).**

• CONCLUSION: **In this population-based study of children with intermittent exotropia, myopia was calculated to occur in more than 90% of patients by 20 years of age. Observation versus surgical correction did not alter the refractive outcome. (Am J Ophthalmol 2010;149: 503–507. © 2010 by Elsevier Inc. All rights reserved.)**

INTERMITTENT EXOTROPIA, CHARACTERIZED BY AN ACquired, intermittent exodeviation, occurs in approximately 1% of healthy children in the United States[1] and, given its predominance over esodeviations among Asian populations,[2] may be the most prevalent form of strabismus worldwide. Although esotropia has been associated with hyperopia and anisometropia,[3–8] the refractive error of children with divergent strabismus has not been as rigorously studied. The purpose of this study is to describe the refractive error outcomes in a population-based cohort of children diagnosed with intermittent exotropia over a 20-year period.

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From the Department of Ophthalmology (N.S.E., K.J.N., B.G.M.) and Division of Biostatistics (N.N.D.), Mayo Clinic and Mayo Foundation, Rochester, Minnesota.

Inquiries to Brian G. Mohney, Mayo Clinic, Department of Ophthalmology, 200 First St Southwest, Rochester, MN 55905; e-mail: mohney@mayo.edu

METHODS

THE MEDICAL RECORDS OF ALL PATIENTS YOUNGER THAN 19 years who were residents of Olmsted County, Minnesota, when diagnosed by an ophthalmologist as having intermittent exotropia between January 1, 1975 and December 31, 1994 were retrospectively reviewed. Institutional review board approval was obtained for this study. Potential cases of intermittent exotropia were identified using the resources of the Rochester Epidemiology Project, a medical record linkage system designed to capture data on any patient–physician encounter in Olmsted County, Minnesota.[9] The racial distribution of Olmsted County residents in 1990 was 95.7% Caucasian, 3.0% Asian American, 0.7% African American, and 0.3% each for Native American and other. The population of this county (106 470 in 1990) is relatively isolated from other urban areas, and virtually all medical care is provided to residents by Mayo Clinic, Olmsted Medical Group, and their affiliated hospitals. Patients not residing in Olmsted County at the time of their diagnosis were excluded. Intermittent exotropia was defined in this study as an intermittent distance exodeviation of at least 10 prism diopters (PD) without an underlying or associated neurologic, paralytic, or anatomic disorder.

Data abstracted from the medical records included gender, family history of strabismus, birth weight, gestational age at birth, reported age at onset, and ocular findings. The angle of deviation was primarily determined by the prism and alternate cover technique at both distance and near, although some younger patients were measured by the Hirschberg or modified Krimsky techniques at near. The initial and subsequent refractions were determined in the majority of patients following the topical administration of 1% cyclopentolate in younger patients and by a manifest refraction for older patients. All refractions were converted into their spherical equivalent. Since no patient had greater than 1 diopter of anisometropia, the refractive errors of the right and left eyes were averaged. Myopia was defined in this study as more than or equal to −0.50 diopters. Follow-up was measured from the date of the initial refraction to the last examination at which the refractive error was recorded through August 31, 2007.

Continuous data are presented as a mean with a standard deviation and categorical data are presented as counts and percentages. Progression of refractive error was determined by measuring the difference between the initial and final refraction divided by the total follow-up time per patient through

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TABLE 1. Historical and Initial Clinical Characteristics of 135 Children With Intermittent Exotropia With 2 or More Refractive Error Measurements

Characteristics	Findings
Number of boys (%)/number of girls (%)	44 (33%)/91 (67%)
Mean age at diagnosis in years (range)	5.6 (0.9 to 14.9)
Number (%) with amblyopia	4 (3%)
Mean initial horizontal deviation at distance in prism diopters (range)	20 (10 to 40)
Mean initial horizontal deviation at near in prism diopters (range)	14 (0 to 45)
Number (%) with inferior oblique dysfunction	19 (14%)
Number (%) with dissociated vertical deviation	3 (2.2%)
Number (%) managed with over-minus correction	6 (4.4%)
Number (%) managed with surgical correction	54 (40%)
Mean follow-up in years (range)	10.1 (1.0 to 27.1)

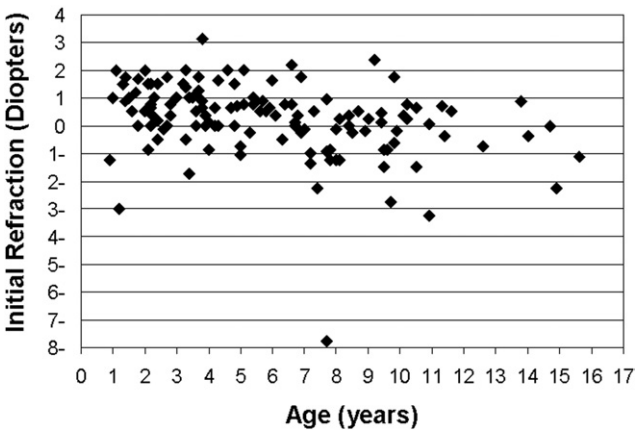

FIGURE 1. Initial refractive error by age in 135 children with intermittent exotropia.

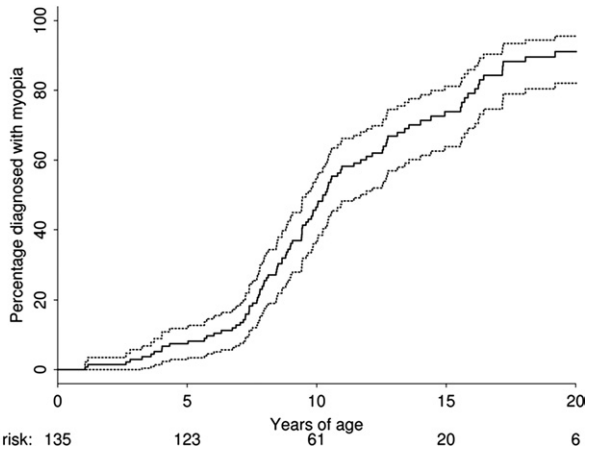

FIGURE 2. Kaplan-Meier estimate of myopic progression by age (with 95% CI) in 135 children with intermittent exotropia.

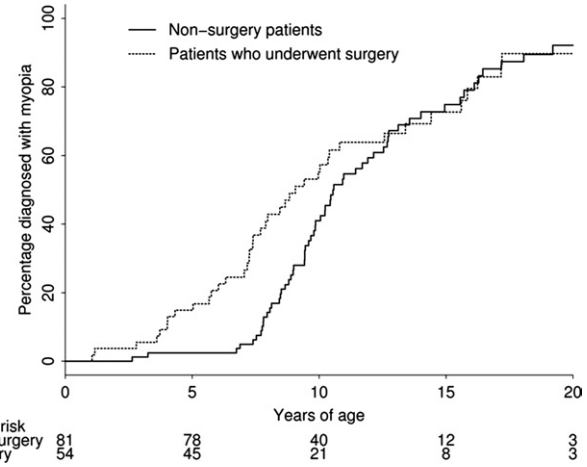

FIGURE 3. The Kaplan-Meier rate of myopic progression between 54 IXT patients who underwent surgery and 81 who were observed ($P = .16$).

the age of 21 years. Comparisons between groups for continuous variables were completed using Wilcoxon rank sum tests and for categorical variables using Fisher exact tests. All statistical tests were 2-sided, and the threshold of significance was set at $P = .05$. The rate of developing myopia was estimated using the Kaplan-Meier method.[10]

RESULTS

ONE HUNDRED EIGHTY-FOUR PATIENTS WERE DIAGNOSED with intermittent exotropia during the 20-year period. One hundred thirty-five of the 184 (73.4%) had 2 or more refractive error measurements separated by at least 1 year, the clinical findings of which are shown in Table 1. There were 44 (33%) male and 91 (67%) female patients. The mean age at diagnosis for the 135 was 5.6 years (range, 0.9 to 14.9 years). Amblyopia was present in 4 patients (3%). The mean initial angle of deviation was 20 prism diopters (range, 10 to 40 PD) and 14 PD (range, 0 to 45 PD) at distance and near, respectively.

The initial refractive error of the 135 children is shown in Figure 1, with a mean value of +0.26 (range, −7.75 to +3.13) at a mean age of 5.6 years. Eighty-four patients (62.2%) were initially hyperopic at an average age of 5.0 years; 56 of them (67%) had less than 1 diopter of hyperopia. Thirty-nine of the 135 patients (28.9%) were initially myopic at a mean age at diagnosis of 7.6 years. The remaining 12 patients (8.9%) were plano at an average age of 5.2 years.

The study patients were followed for a mean of 10.1 years (range, 1.0 to 27.1 years). The final refractive error of the 135 children included myopia in 95 (70%), hyperopia in 34 (25%), and plano in 6 (4.4%), at a mean age of 15.9

TABLE 2. Published Reports of Mean Initial Refractive Error in Patients With Intermittent Exotropia

Author(s)	Number of Patients	Mean Age at Initial Examination in Years	Mean Initial Horizontal Deviation in Prism Diopters	Mean Initial Refractive Error in Diopters
Kushner[11]	62	4.4	28	plano ± 1.40
Caltrider and Jampolsky[12]	15	6.9	Not specified	−0.669 (−3 to +1.75)
Current study	135	5.6	21	+0.26 (−7.75 to +3.13)

TABLE 3. Published Reports of Myopia Prevalence in Cohorts of Children by Age Range

Author(s)	Country of Study	Age Range in Years	Sample Size	% with Myopia	Kaplan-Meier Rate of Myopia Prevalence (%) in our Population
Preslan and Novak[13]	United States	4 to 7	680	3.1	8.8
Zadnik and associates[14]	United States	6 to 14	716	7.5	43.0
Grosvenor[30]	Vanuatu	6 to 19	788	2.9	57.3
Cummings[31]	United Kingdom	8 to 10	1809	24.4	36.1
Auzemery and associates[32]	Madagascar	8 to 14	1081	0.92	52.1
Lin and associates[33]	Taiwan	13 to 16	2353	49.6	72.5
Angle and Wissmann[15]	United States	12 to 17	13 536	31.8	72.6
Au Eong and associates[34]	Singapore	15 to 25	110 236	44.2	88.7

[a]The percentage presented was calculated based on the mean Kaplan-Meier rate for each age in the range specified.

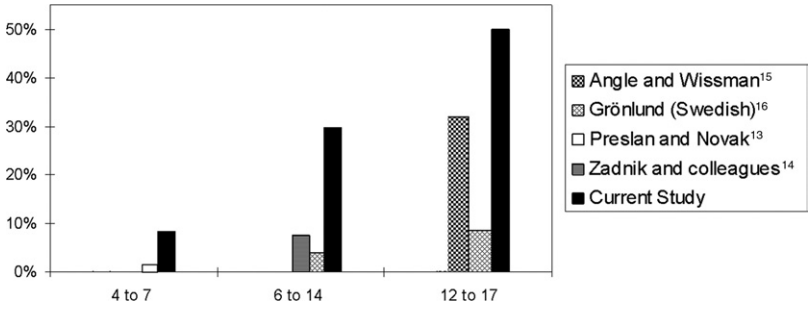

FIGURE 4. A comparison of the prevalence of myopia by age from this study with published reports of normal populations from the United States.

years. The Kaplan-Meier rate of developing myopia in this population was 7.4% by 5 years of age, 46.5% by 10 years, and 91.1% by 20 years (Figure 2). Of the 135 children, 54 (40%) underwent surgical correction for IXT. The Kaplan-Meier rate of developing myopia in the surgery group versus the observation group is shown in Figure 3. There was no significant difference in the rate of myopic progression between the two groups ($P = 0.16$). Only 6 patients were treated with over-minus correction, but this group was too small for any statistical analyses.

To calculate the annual myopic progression, a subset of patients with 2 or more refractive error measurements separated by at least 1 year *and* measured before the age of 21 years was reviewed. One hundred and six patients met these criteria with a mean follow-up of 8.2 years (range, 1.0 to 18.8 years). The annual overall progression for the 106 patients was −0.26 diopters (SD ± 0.24). In the 54 patients who underwent surgical correction, the rate of progression was −0.25 diopters (SD ± 0.23) versus −0.27 (SD ± 0.25) in those who were merely observed ($P = .59$).

DISCUSSION

THE FINDINGS FROM THIS POPULATION-BASED STUDY OF 135 children with intermittent exotropia (IXT) showed a significant trend toward myopia over time. The Kaplan-Meier rate of developing myopia in this population was 7.4% by 5 years of age, 46.5% by 10 years, and 91.1% by 20 years. Whether or not a patient underwent

surgical correction did not appear to have an impact on his or her rate of myopic progression.

The initial refractive error of our population of children with intermittent exotropia is comparable to published reports of patients with IXT (Table 2). Kushner reported an average refractive error of plano for 62 exotropic children at a mean age of 4.4 years.[11] Caltrider and Jampolsky reported a mean refractive error of −0.669 in 15 children at a mean age of 6.9 years.[12] Although similar to reports in patients with IXT, the prevalence of myopia in our population was markedly higher than published reports of children surveyed in a general population (Table 3). In the United States, Preslan and Novak reported a myopia (≤−0.75 diopters) prevalence of 3.1% in their population of 4- to 7-year-olds residing in Baltimore, Maryland.[13] Zadnik and associates, describing a population of 6- to 14-year-olds, found myopia (≤−0.75 diopters) in 7.5% of their patients.[14] Angle and Wissmann reported that 31.8% of 12- to 17-year-olds examined by the U.S. National Health Survey were myopic (≤−1.0 diopters).[15] As shown in Figure 4, our cohort of patients with intermittent exotropia had a far greater prevalence of myopia compared to similarly aged American children reported by these authors. Since the population in Olmsted County has a high rate of Scandinavian ancestry, we also included a Swedish population reported by Grönlund and associates[16] in Figure 4.

A number of factors have been associated with myopic progression, including ethnicity, birth during summer months, female gender, younger baseline age at onset, high IQ scores, prolonged study time, and parental myopia.[17–22] Although we did not examine the IQ of study patients or the prevalence of parental myopia, two-thirds of the children in this study were female,[23] which may partially explain the high rate of myopic progression. However, the birth months of our study patients were not significantly concentrated in the summer. The elevated risk associated with a younger age at baseline and Asian ethnicity were also not factors for our population. While it is well known that myopia is prevalent among Asian populations (Table 3), it is interesting to note that exotropia is also at least twice as common as esotropia in Asia,[2,24] while the reverse is true for Western populations. However, it is unknown why the Caucasian children with IXT in this study, whose mean initial refractive error was hyperopic, developed myopia as fast as or faster than that described for Asian populations (Table 3).

There are several potential explanations for the association between IXT and myopia. A relationship between outdoor activity and less myopia coupled with increased myopia among children performing extended near work has recently been reported.[19,20,25,26] It could be argued that children living in the colder climate of Minnesota are more likely to stay indoors performing near work, thereby enhancing their potential for developing myopia. However, this finding was not seen among children residing in the similarly cold climate of Sweden.[16] Also, children with IXT are likely to have more frequent ophthalmic examinations, potentially leading to an earlier diagnosis and correction of myopia. This close observation and possible early correction may adversely alter emmetropization. The increased accommodative demand in children with intermittent exotropia may be another factor.[27] Chua and associates have shown that the reduction of accommodation with atropine eye drops slowed the progression of moderate myopia and axial elongation in Asian children.[28] However, additional investigations have shown an increase in progression of myopia after the discontinuation of atropine.[29] Further study is needed to clarify the relationship between myopia, accommodation, and IXT. While we are unable to state that IXT causes myopia, they appear to be significantly linked and intermittent exotropia may be a risk factor for myopic progression.

There are a number of limitations to the findings in the current study. Its retrospective nature is limited by imprecise inclusion criteria and unequal follow-up. We attempted to overcome the latter weakness by employing the Kaplan-Meier method to estimate the rate of myopic progression. Second, not all refractions were performed with a cycloplegic agent. However, the mean age at the final refraction for the 135 study patients was 18 years, an age at which a cycloplegic refraction is uncommonly performed for patients with myopia. We also could not determine the precise age at myopia onset since patients would often have myopia of varying degrees on presentation. For these reasons, myopic progression was determined from the date at diagnosis rather than the age at onset, which is difficult to determine for any patient with refractive error. Moreover, although the study patients represent a population-based cohort, we were unable to identify a representative control group from the same population with which to compare our refractive error findings. Additionally, although the region is relatively isolated, some exotropic residents of Olmsted County may have sought care outside of the region, thereby potentially biasing the study population. Finally, the demographics of Olmsted County limit our ability to extrapolate the findings from this study beyond other semi-urban white populations of the United States.

This study provides population-based refractive error data on 135 children with intermittent exotropia diagnosed over a 20-year period. More than 90% of patients were calculated to become myopic by early adulthood, a rate that is much higher than the general U.S. population and nearly double that of the Asian communities in which myopia and exotropia are more prevalent. These findings, which require confirmation elsewhere, demonstrate an association between intermittent exotropia and myopia.

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Institutional review board approval from the Mayo Clinic and the Olmstead Medical Group was obtained for this study.

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