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Refractive Error Development in Children with Intermittent Exotropia

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ABSTRACT

Background and Objective: Intermittent exotropia is the most common type of outward deviation of the eye in childhood. The association between myopia refractive error and intermittent exotropia has been shown in very few studies. This study was conducted to investigate the association between various refractive errors and the course of their changes in patients with intermittent exotropia.

Methods: This retrospective study was conducted on 130 patients with intermittent exotropia younger than 16 years of age who referred to Khatam-al-Anbia Eye Hospital in Mashhad. The records of patients with follow-up were reviewed in terms of age, gender, and near and distance angles of deviation using cover test, type and grade of refractive errors at the initial visit and subsequent visits using cycloplegic drops, types of treatments performed, and dominance of the patients' eyes. Changes in refractive errors during different visits in the patients were examined and compared.

Findings: The mean age of the patients was 5.64±4.08 years, of which 77 (59.2%) were girls. The mean distance deviation angle of the patients was 30.79±12.13 prism diopters and the mean near deviation angle was 24.27±17.85 prism diopters. The most common treatment performed for the patients was patch therapy (57.4%). At the initial visit, 77 patients (54%) were hyperopic. In the non-dominant eye, changes in refractive errors towards a decrease in spherical refraction were significant (p=0.002).

Conclusion: The results of this study showed that most patients were hyperopic and the course of changes was towards a decrease in spherical equivalent (shift towards myopia).

Keywords: *Intermittent Exotropia, Myopia, Refractive Errors.*

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Introduction

Intermittent exotropia, which involves intermittent outward deviation of the eyes, is one of the most common types of outward deviation in children (1, 2). This deviation accounts for 50-90% of exotropia cases. It usually manifests before the age of five and is more prevalent in women and Asians (3, 4). In addition to its unpleasant functional effects such as reduced depth perception and amblyopia, patients with exotropia face issues such as anxiety, depression, decreased self-confidence, dissatisfaction in communicating with others, social judgments, and diminished quality of life (5, 6). Although the etiology of intermittent exotropia is unclear, factors such as genetics, neurological factors, family history, and refractive errors have been proposed for it (7, 8). Intermittent exotropia at larger angles causes eye fatigue and amblyopia and impaired binocular vision in patients (9).

Although inward deviation (esotropia) is associated with hyperopia due to accommodation, the results of studies investigating the association of different types of refractive errors with intermittent exotropia are diverse (8, 10). Some have reported a normal distribution of refractive errors in these patients (1), while others have indicated a high prevalence of myopic refractive errors in patients with intermittent exotropia (11, 12). In Asia, myopia has been reported to be more prevalent in children with intermittent exotropia than with esotropia (43%) (3). A 20-year study showed that more than 90% of patients with intermittent exotropia become myopic by the age of 20 (13).

Increased accommodation requirements to control exotropia have been suggested as a risk factor for myopia progression in some studies. However, other factors such as eye dominance and therapeutic interventions such as surgery and prescription of minus lenses in patients with intermittent exotropia have also been shown to be associated with myopia progression (14). Despite limited studies in this area, some other studies have indicated no association between myopia progression and intermittent exotropia (15, 16). Therefore, the results of studies in this area are still contradictory (16, 17).

Understanding the relationship between refractive errors and intermittent exotropia will further help in understanding the pathology of the deviation and, consequently, its better management. Therefore, this study was conducted to investigate the association between different types of refractive errors and the course of their changes in patients with intermittent exotropia.

Methods

After approval by the Ethics Committee of Mashhad University of Medical Sciences with the code IR.MUMS.fm.REC.1396.561, this retrospective cohort study was conducted on all patients with intermittent exotropia younger than 16 years of age who referred to the specialized strabismus clinics of Khatam-al-Anbia Eye Hospital in Mashhad. Information related to the patients' intermittent exotropia deviation, including age, gender, near and distance angles of deviation, grade of refractive errors, treatments performed to control the deviation, and eye dominance in patients with at least one year of follow-up, was collected. Cases of anatomical, neurological, and paralytic disorders related to exotropia deviation, and the presence of corneal and retinal diseases were among the exclusion cases.

The diagnosis of intermittent exotropia was made by an ophthalmologist with at least 10 prism diopters at a distance (6 meters) in the cover test. The angle of deviation was measured at distance (6 meters) and at near (33 cm) by cover test and prism method and recorded based on prism diopter units. The patient's deviation control was qualitatively assessed in the cover test and recorded at three levels: good, moderate, and poor. Good control was defined as deviation appearing only during the cover test and the eyes returning without blinking, moderate control was defined as deviation appearing during the cover test and the eyes

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returning to the non-deviation phase after blinking, and poor control was defined as deviation appearing at the same time as the cover test and remaining in the deviation phase. Also, to examine the dominance of the eyes, the eye that took the shortest time to return to its fixation in the test cover was considered as the dominant eye.

Refractive errors were assessed by examination using cycloplegic eye drops and recorded as spherical equivalent (cylinder divided by two plus spherical coordinates). Refractive errors were defined as spherical equivalent according to the study by Negrel et al. (18). In defining the type of refractive error, myopia was considered as spherical equivalent ≤-0.5 diopters, hyperopia was considered as spherical equivalent ≥0.5 diopters, anisometropia was considered as spherical equivalent difference between the two eyes ≥1 diopter, and astigmatism was considered as values higher than one diopter (<1) in each eye.

Data were analyzed using SPSS software. Descriptive statistical methods including central tendency, dispersion, and frequency distribution were used to describe the data. Qualitative variables were described by frequency and percentage, and quantitative variables were described by mean and standard deviation. Chi-square test was used to compare qualitative variables. Independent t-test or its nonparametric equivalent was used to compare quantitative variables. Repeated-measures analysis of variance or its nonparametric equivalent was used to compare changes in refractive errors and the angle of eye deviation in subsequent follow-ups, and $p<0.05$ was considered significant.

Results

In this study, the files of 130 patients with intermittent exotropia with a mean age of 5.64±4.08 years were evaluated. 77 patients (59.2%) were girls. The mean distance deviation angle of the patients was 30.79±12.13 prism diopters and the mean near deviation angle of the patients was 24.27±17.85 prism diopters (Table 1). 57.6% of the patients had poor deviation control, 15.3% had moderate control, and 27.1% had good control. No significant difference was observed between the type of refractive error and deviation control.

At the first visit, 77 (54.6%) patients were hyperopic, 26 (20%) were myopic, and 61 (47%) patients had some degree of astigmatism. 19 (14.61%) patients had anisometropia. The mean age of hyperopic patients was 2.4±2.9 years, myopic patients were 6.5±4.5 years, and emmetropic patients were 9.6±2.5 years. The mean and standard deviation of corrected visual acuity in the right eye was 0.11±0.19 LogMAR and in the left eye was 0.11±0.17 LogMAR.

Among the treatments performed in this study, which included observation, patch therapy, prescription of glasses with minus lenses (Overminus spectacles), and surgery, patch therapy was prescribed to the patients in the highest percentage (57.4%), followed by prescription of glasses with minus lenses (39.5%), surgery (30.23%), and finally observation (11.5%) (Figure 1).

The spherical equivalent was 0.8±2.35 diopters in girls and 0.09±2.69 diopters in boys, and there was no significant difference between the two genders. The spherical equivalent was 0.77±1.45 diopters in the age group less than 7 years and 0.65±13.3 diopters in the age group more than 7 years, with no significant difference.

In evaluating the course of changes in refractive errors, the average time interval between visits from baseline to first visit was 9.89±10.69 months, first visit to second visit was 14.91±17.70 months, and second visit to third visit was 15.35±11.45 months. The average baseline spherical equivalent in the right eye was 1.07±2.80 diopters and in the left eye was 0.72±3.60 diopters, which showed a significant decrease in spherical equivalent (shift towards myopia) in the follow-up visits ($p=0.02$ and $p=0.003$, respectively) (Figure 2).

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Table 1. Characteristics of the study subjects (n=130)

Variable	Mean±SD or Number(%)
Age (years)	5.64±4.08
Gender	
Girl	77(59.2)
Boy	53(40.8)
Dominant eye	
Right eye	50(38.5)
Left eye	50(38.5)
Intermittent	30(23)
Deviation angle (prism diopter)	
Distance	30.79±12.13
Near	24.27±17.85

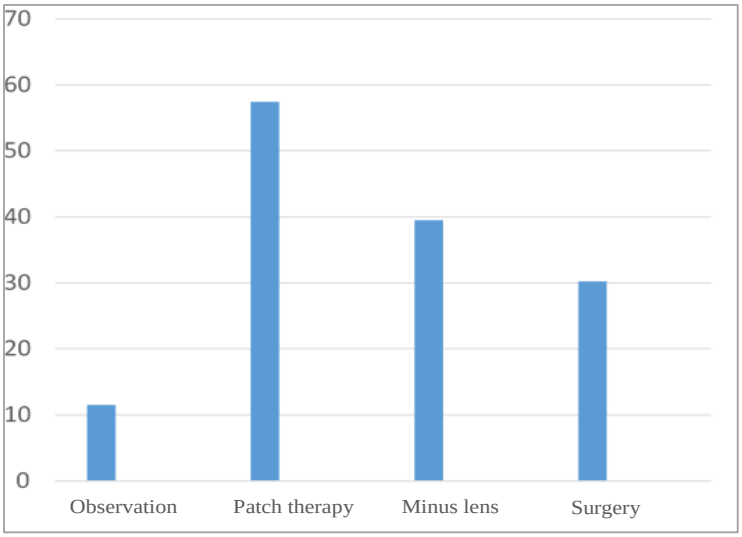


Figure 1. Percentage frequency of different treatment methods for intermittent exotropia

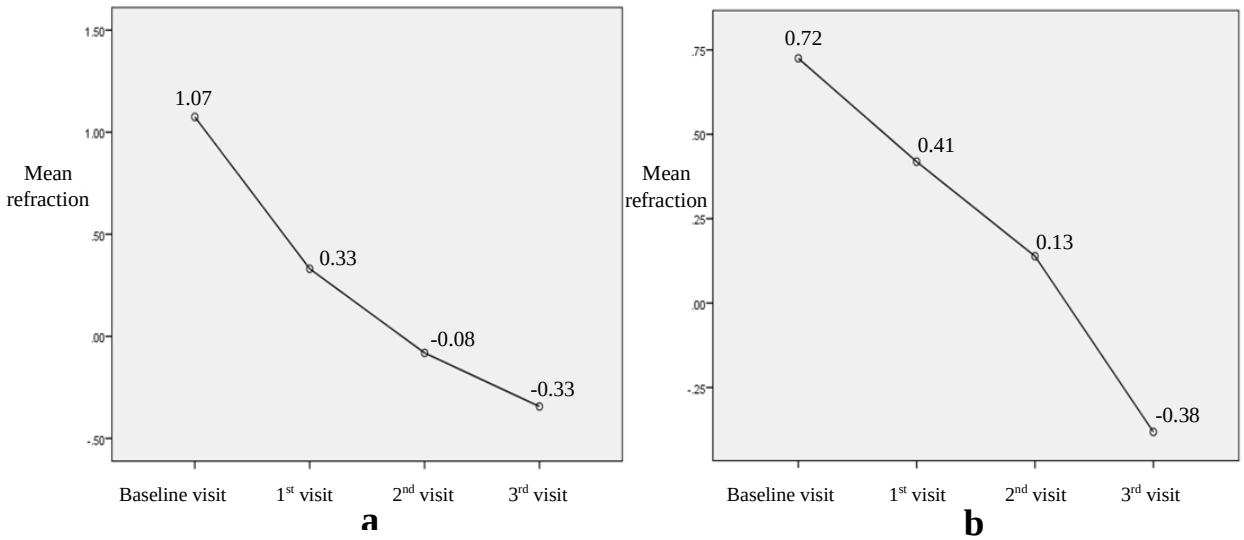


Figure 2. Diagram of the course of refraction changes during visits in the right eye (a) and left eye (b)

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In examining the course of changes in spherical equivalent in the dominant eye, the changes during follow-ups were not significant, while in the non-dominant eye, the changes showed a significant decrease (shift towards myopia) (p=0.002) (Table 2).

In comparing the changes in the angle of eye deviation at different visits, a significant decrease was observed in both distance and near vision (Table 3). In comparing the baseline characteristics of patients who underwent surgery and those who did not undergo surgery, the group that underwent surgery was significantly older than the non-surgical group (6.84±4.88 and 5.06±3.56, respectively, p=0.02). Also, in patients who underwent surgery, near deviation angle at baseline showed a significant difference from those who did not undergo surgery (31.45±15.38, and 17.18±15.23 prism diopters, respectively, p=0.02). However, distance deviation angle and spherical equivalent refraction at baseline did not show a significant difference between these two groups (p=0.3, p=0.77, respectively) (Table 4).

Table 2. Course of changes in spherical equivalent by dominant and dominant eye

Parameters	Dominant eye (diopter) Mean±SD	Non-dominant eye (diopter) Mean±SD
Baseline visit	0.75±2.21	1.55±3.21
First visit	0.71±2.29	1.44±3.35
Second visit	0.33±2.69	0.95±3.37
Third visit	0±3.23	0.55±3.8
p-value*	0.09	0.002

*Repeated measure test

Table 3. Changes in the angle of deviation in different visits

Parameters	Distance deviation angle (prism diopter) Mean±SD	Near deviation angle (prism diopter) Mean±SD
Baseline visit	30.79±12.13	24.27±3.56
First visit	29.93±11.98	21±13.77
Second visit	23.95±13.38	11.9±11.42
Third visit	16.81±13.03	12.27±12.1
p-value*	<0.001	0.001

*Repeated measure test

Table 4. Baseline characteristics of patients with and without surgery

Parameters	Surgery (n=40) Mean±SD	Non-surgery (n=90) Mean±SD	p-value*
Age (years)	6.84±4.88	5.06±3.56	0.02
Distance deviation angle (prism diopter)	31.47±12.16	28.49±15.03	0.30
Near deviation angle (prism diopter)	31.45±15.38	17.18±15.23	0.02
Spherical Equivalent (Diopter)	0.83±1.94	0.68±2.44	0.77

*Independent t-test

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Discussion

In this study, the course of changes in refractive errors in patients with intermittent exotropia showed a shift towards a decrease in the spherical equivalent (shift towards myopia). This decrease was also significant in the non-dominant eye compared to the dominant eye. Most children with intermittent exotropia participating in this study were girls (59.2%), which is in agreement with the results of the study by Nusz et al. (19). By examining intermittent exotropia patients younger than 19 years, they concluded that this deviation was twice as high in girls, although they did not observe other differences in terms of family history or refractive errors between the two genders, which is in accordance with our observation in this study and no significant difference was observed between the two genders in terms of refractive errors.

The decrease in spherical equivalent refraction in this study was consistent with the results of previous similar studies (13, 20). In the study of Ekdawi et al., it was shown that at the initial visit, the most common refractive error in patients was hyperopia (62%), followed by myopia (29%), and finally emmetropia (8%) (13). In our study, most patients were hyperopic (54.6%) at the initial visit. They also showed that more than 90% of patients with intermittent exotropia become myopic by the age of 20 and suggested intermittent exotropia as a risk factor for the progression of myopia (13). In a meta-analysis, Tang et al. reported that myopic children have a 23.5-fold increased risk of exotropia (8), which could be due to the high prevalence of exotropia and myopia in Asia. Although the exact mechanism of the relationship between myopia and exotropia is still unknown, it is suggested that the control of distance deviation in myopic individuals is poor due to distance blur, and in near vision, due to the larger accommodation lag in them, less accommodation effort is required for clear images, which can lead to reduced accommodation convergence and ultimately convergence insufficiency (21, 22).

This lower convergence in the long term may lead to failure of deviation control and may cause exotropia. In a study conducted by Kim et al., they concluded that an overall shift towards myopia in spherical equivalent was observed at 10-year follow-up. They suggested that among various factors such as ocular aberrations, primary refractive errors, gender, and astigmatism, primary refractive errors were the most predictive factor for myopic shift (23). On the other hand, in a recent study by Oruz et al., myopia progression was greater in children with intermittent exotropia under 19 years of age compared to the normal population (11). This progression could be due to reasons such as increased accommodation needs in intermittent exotropia patients (16, 17, 24, 25). However, there are studies with diverse results (16). In a study by Zhu et al., it was reported that there is a strong relationship between mild to moderate hyperopia and exotropia (10).

In a recent study by Shen et al., no significant difference was observed in the rate of myopia progression between normal children and children with intermittent exotropia, and a shift toward myopia was generally observed in all participants (12). Shin et al. showed that myopia progression was similar between exotropia and control children. This is despite the fact that all participants in their study were myopic (16). Patients with intermittent exotropia with any type of refractive error and a mean age of 5.64 years participated in our study. The contradictory results of studies about myopia and intermittent exotropia may be due to the multifactorial nature of myopia. Changes in refractive errors have a complex course and can be influenced by a range of factors such as genetics, race, age, gender, initial refractive errors and ocular aberrations, and environmental factors such as education, and outdoor activities. Given the limited studies conducted in this field, their cross-sectional nature, different groupings and age ranges, and limited sample size, and the fact that the interaction between these factors is not yet fully understood, controlled studies of factors involved in the progression of myopia are recommended.

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Eye dominance, which is the preference of visual information from one eye over the other in binocular vision, has been shown in some studies to affect myopia progression (26). In a study by Moon et al., it was shown that the dominant eye progresses myopia more rapidly than the dominant eye in patients with intermittent exotropia (27). However, their study was conducted on patients who had undergone deviation surgery. Shen et al. did not observe a difference in the course of myopia changes between the dominant and dominant eyes (12). In our study, the course of spherical equivalent changes in the non-dominant eye at referrals showed a significant decrease compared to changes in the dominant eye. Knowledge of the status of the dominant eye in patients with exotropia helps in better management of the deviation, including the selection of the eye for patch therapy or surgery. However, studies in this regard are limited and have conflicting results.

Anisometropia, which is the difference in refractive errors between the two eyes, can lead to a further decrease in binocular vision in people without astigmatism (28). In our study, the rate of anisometropia was 14%. Also, nearly half (47%) of the patients showed varying degrees of astigmatism. Various studies have reported a relationship between astigmatism and exotropia (10), and even the role of correcting small amounts of astigmatism has occasionally been shown in better control of exotropia. However, there are also studies that did not observe a relationship between astigmatism and anisometropia with exotropia deviation (10, 13), which could be due to various reasons, including different definitions of the degree of astigmatism and anisometropia in the studies.

The most common treatment for patients in this study was patch therapy (57.4%). Treatment of intermittent exotropia is often performed with surgical and nonsurgical interventions that include patch therapy, observation, and prescription of minus lenses and orthoptic eye exercises. However, the relative effectiveness of these treatments has not been studied in detail. In this study, 39.5% of patients were prescribed minus lenses. Prescription of minus lenses is an effective nonsurgical method for intermittent exotropia. However, whether prescription of these lenses causes myopia progression in patients with intermittent exotropia is unknown. In a study by Ale Magar et al., no difference in the development of refractive errors was observed between exotropia patients who used minus lenses and those who did not (29). In a clinical trial among children aged 3–10 years, an increased shift toward myopia was observed in the minus lens group compared to the non-minus lens group, especially in those who were myopic from the beginning (30). In a study by Oruz et al. in children younger than 19 years with intermittent exotropia, there was no significant difference in myopia shift between the minus lens group and the observation group (11). Theoretically, the increased need for accommodation following prescription of minus lens glasses may cause myopia. However, the results are contradictory and further studies are needed.

In the present study, 30% of the patients had undergone surgery. In the study by Shin et al., it was shown that the rate of myopia progression was not different in patients with intermittent exotropia who underwent surgery, and patients with intermittent exotropia and myopia did not show a difference in myopia progression compared to those who were only myopic (16). There are also studies that show faster myopia progression in intermittent exotropia surgery (14) and sometimes report a transient shift towards myopia (12). On the other hand, hyperopia has been shown to be less desirable than myopia in the results of intermittent exotropia surgery (31). In the present study, there was no difference between the baseline spherical equivalent refraction of the two groups who underwent surgery and those who did not. The patients who underwent surgery were older and had a larger near deviation angle. The age of surgery for intermittent exotropia and the results of surgery are inconsistent in studies. In general, it is recommended to perform

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surgery at an appropriate time. Some studies have suggested older ages to allow for more accurate measurement and monitoring of progress, while others have suggested performing surgery at younger ages to preserve binocular vision. There are also studies that have shown that the role of age at surgery is irrelevant in the results of surgery (32).

One of the strengths of this study is the use of refractive error findings related to intermittent exotropia patients with follow-up and refractive error examinations with drops (which is considered the gold standard in pediatric refractive error examinations). However, limitations such as retrospective nature, lack of a control group without deviation, and single-center design are limitations of the present study and cannot be generalized to the entire population.

The results of this study showed that most patients with intermittent exotropia had a refractive error of hyperopia type at the beginning of the visit, and showed a decrease in the rate of spherical equivalent (shift towards myopia) in the follow-up, and this decrease was significant in the non-dominant eyes. Prospective cohort studies with a larger population and examining the effect of dominance of the eyes and different treatment methods of intermittent exotropia with the progression of myopia are recommended.

Conflict of interest: There are no conflicts of interest.

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