Factors Predisposing to Amblyopia After Exotropia Surgery

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Abstract- Amblyopia (lazy eye) is one of the significant complications of strabismus surgery. It is the most important cause of unilateral visual impairment in both children and adults. The current investigation was achieved to determine the postoperative amblyopia rate and to identify factors predisposing to amblyopia following exotropia surgery among patients who had been referred to Imam Khomeini Hospital in Urmia, Iran. The present investigation is a retrospective study that was conducted over three years (2008-2010). The study consisted of sixty patients who underwent their first strabismus surgery for treatment of horizontal deviation. Patients were followed up for at least 24 months, and the rate of postoperative amblyopia was measured. The preoperative deviation, strabismus type (exotropia vs. esotropia), visual acuity, age at surgery, and the number of operated muscles were analyzed as determining factors of postoperative development of amblyopia. Amblyopia was observed in 50% of cases during the follow-up period. No statistically significant differences were observed between amblyopic and non-amblyopic eyes in terms of sex, age at surgery, strabismus type, and visual acuity. But amblyopic eyes showed higher deviation angles compared to non-amblyopic eyes (<0.001). The Cox hazard model analysis revealed a significant contribution of deviation angle to postoperative development of amblyopia. A larger deviation angle has been identified as a positive predictor of postoperative development of amblyopia in our investigated population. Due to such a high rate of postoperative amblyopia, it seems better to initiate and complete amblyopia therapy before strabismus surgery.

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Keywords: Strabismus; Exotropia; Amblyopia; Deviation angle; Postoperative

Introduction

Strabismus is a disorder of ocular alignment characterized by a vertical, horizontal, or torsional deviation of one eye relative to the other. This disease is a common problem in ophthalmology, occurring in 3-4% of the population (1). Based on the time of onset, strabismus can be classified as congenital or acquired. Anatomical defects, cranial nerve palsy, cataract, raised intracranial pressure, head or orbital traumas, brain infections, vascular and brain lesions, refractive errors, and visual loss are among the common etiological factors of acquired strabismus (2). Whereas family history, advanced maternal age, cigarette smoking during pregnancy, low birth weight, and immaturity have been recognized as risk factors for infantile strabismus (3-4). According to the direction of the eye misalignment, there are four common types of strabismus, including esotropia, exotropia, hypotropia, and hypertropia (5).

Strabismus surgery is usually performed when misalignment of the visual axes can no longer be treated with conservative measures such as eye patching, eyeglasses, orthoptic exercises, and prisms (6). This procedure loosens or tightens extraocular eye muscles and therefore modifies the alignment of the eyes relative to each other. However, some complications are associated with strabismus surgery, including amblyopia, diplopia, secondary misalignments, suture sensitivity, postoperative infections, Dellen formation, conjunctival cyst or scars, and blepharoptosis (7-8).

Amblyopia, also known as lazy eye, is usually defined as a reduction in corrected visual acuity (VA) in one or both eyes, without any visible structural or

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pathological anomalies (9). It is the most important cause of unilateral visual impairment in both children and adults (10-12) and accounts for 50% to 73% of all such vision loss (13-16). Strabismus has been identified as the major cause of amblyopia (about 50% of cases). The other causes are anisometropia (about 17%), a combination of strabismus and anisometropia (approx. 30%) and visual deprivation (≤3%) (17-18).

The primary objective of this study was to determine the postoperative amblyopia rate and to identify factors predisposing to amblyopia following exotropia surgery among patients who had referred to Imam Khomeini Hospital in Urmia, Iran.

Materials and Methods

In the current investigation, the medical files of patients who underwent exotropia surgery at Imam Khomeini Hospital from April 2008 to March 2010 were reviewed retrospectively. All deviations were treated by one ophthalmologist (NSA) with recession/resection (R & R) technique. According to the preoperative exodeviation angles, subjects received surgery on two (those with 60-70 PD), three (those with 70-80 PD) or four muscles (those with>80 PD). None of the included cases had the experience of strabismus operation before. Refractive errors, history of amblyopia treatment prior to surgery, chromosomal anomalies such as Down syndrome and history of cataract or glaucoma surgery were accepted as exclusion criteria. This investigation was approved by Human Ethics Committee at the Medical University of Urmia and Health Services, Urmia, Iran.

Data regarding age at surgery, sex, visual acuity, strabismus types (exotropia vs. esotropia), pre- and postoperative deviation angles and postoperative amblyopia rate were all retrieved from medical records. All included cases were followed up for at least 24 months and 35% (21 cases) were followed up for 3 years. Amblyopia was defined as an interocular difference of more than one Snellen type line between the two eyes.

Primary data were processed using SPSS software, version 17. Qualitative variables were presented by absolute and relative frequencies whereas, quantitative variables were presented as mean±standard deviation (SD). Fisher exact test and Mann-Whitney U-test were utilized to analyze binary and continuous data respectively. The significance of patient age, gender, strabismus type (exotropia or esotropia), angles of deviation, the number of operated muscles, and visual acuity as predictive factors of postoperative development of amblyopia were determined by Cox proportional hazard model. Two-sided $P<0.05$ were assumed to be statistically significant.

Results

Sixty patients (29 males and 31 females) who had undergone an exotropia surgery were included in the present study. Demographics and preoperative characteristics of patients are presented in Table 1. The mean age of patients at the time of surgery was 21.05±10.91 years (median=17 years; range=4-63 years). 48.3% of patients (29 individuals) had less than 20 years of age at the time of surgery. 68.3% (41 cases) of patients suffered from esotropia, while 31.7% of cases (19 individuals) had exotropia. 17 individuals had esotropia in both eyes, whereas 7 patients had been diagnosed with exotropia in both eyes. The mean deviation angle was 53.41±16.65 prism diopters (PD). Two muscles (lateral rectus and medial rectus) were operated on in 20 patients (33.3%), whereas 13 patients (21.7%) received surgery on three muscles. Additionally, 27 cases (45.0%) had all four muscles (2MR and 2LR) operated.

Amblyopia was observed in 50% of cases during the follow-up period. Preoperative characteristics of patients with and without amblyopia are compared in Table 2. No statistically significant differences were observed between the two groups in terms of sex, age at surgery, strabismus type (exotropia vs. esotropia), and visual acuity. Amblyopic eyes had a higher deviation angle in comparison to non-amblyopic eyes (<0.001) (Table 2).

Table 3 displays the results of the proportional hazard analysis. The Cox hazard model method revealed a significant contribution of deviation angle to postoperative development of amblyopia. Indeed, a larger deviation angle has been identified as a positive predictor of amblyopia development (corrected hazard ratio [HR]: 8.255; 95% confidence interval [CI]: 2.221-35.214; $P=0.006$). Other investigated parameters, including sex, age at surgery, visual acuity, strabismus type, and the number of operated muscles, didn't show association with postoperative amblyopia.

The overall estimated median time to postoperative amblyopia in our study was nine months (min: 1, max: 30, mean: 10.23).

Table 1. Demographics and preoperative characteristics of the investigated patients

Characteristics		N=60 cases
Gender, N (%)	Male	29 (48.3)
	Female	31 (51.7)
Age at surgery [yr]	Mean ± SD	21.05±10.91
	Median (min, max)	17 (4, 63)
	Age group 1 (<20 yr)	29
	Age group 2 (20-40 yr)	28
	Age group 3 (>40 yr)	3
Esotropia, N (%)		41
Right eye		8 (19.5)
Left eye		16 (39)
Both eyes		17 (41.5)
Exotropia, N (%)		19
Right eye		7 (36.8)
Left eye		5 (26.3)
Both eyes		7 (36.8)
The angle of deviation preoperative	Mean + SD (prism diopters, PD)	53.41±16.65
	Median (max, min)	39 (25, 90)
Operated muscles, N (%)	2 muscles (those with 60-70 PD)	20 (33.3)
	3 muscles (those with 70-80 PD)	13 (21.7)
	4 muscles (those with >80 PD)	27 (45)
Visual acuity preoperative	Mean + SD	0.612±0.278

Table 2. Comparison of demographics and preoperative characteristics between amblyopic and non-amblyopic patients

Characteristics		Non-amblyopic patients (N=30)	Amblyopic patients, (N=30)	*P*
Gender, N (%)	Male	15 (30)	14 (46.7)	0.999
	Female	15 (30)	16 (53.3)	
Age at surgery [yr]	Mean ± SD	23.56±8.92	18.21±11.79	0.071
	Age group 1 (<20 yr)	11 (36.7)	18 (60)	
	Age group 2 (20-40 yr)	16 (53.3)	12 (40)	0.062
	Age group 3 (>40 yr)	3 (10)	0	
Diagnosis, N (%)	Esotropia	21 (70)	20 (66.7)	0.999
	Exotropia	9 (30)	10 (33.3)	
Angle of deviation preoperative	Mean±SD (prism diopters, PD)	46.43±15.22	59.32±19.44	<0.001
Operated muscles, N (%)	2 muscles (those with 60-70 PD)	8 (26.7)	12 (40.0)	0.567
	3 muscles (those with 70-80 PD)	7 (23.3)	6 (20.0)	
	4 muscles (those with >80 PD)	15 (50.0)	12 (40)	
Visual acuity preoperative	Mean (min, max)	0.658±0.341	0.578±0.221	0.501

Table 3. Adjusted hazard ratios and 95% confidence intervals for the contribution of risk factors to amblyopia

Variable		Adjusted HR (95% CI)	*P*
Age		3.082 (0.740-18.052)	0.061
Sex		2.329 (0.254-29.210)	0.428
Diagnosis		0.886 (0.447-15.474)	0.746
Angles of deviation		8.255 (2.221-35.214)	0.006
Operated muscles	2 muscles compared to 4 muscles	0.643 (0.245-15.345)	0.501
	3 muscles compared to 4 muscles	1.119 (0.491-10.286)	0.625
Visual acuity		0.417 (0.045-1.942)	0.801

Discussion

The amblyopic eye is characterized by the impairment of visual acuity, abnormal contour interaction, positional uncertainty, reduced contrast perception, and inaccurate eye movements, resulting in an extended functional visual loss (19-21). Additionally, unilateral amblyopia is associated with poor binocular

vision, limited employment opportunities, and an increased risk of visual impairment due to acquired disease in the fellow eye (22-23). Prevalence rates of amblyopia ranged from 0.6% to 5.3% in previous studies (24). On the other hand, it has been reported that 1% to 21% of children who have undergone exotropia surgery develop amblyopia (25-27).

There are several studies in the literature that aimed to identify the factors associated with favorable or less favorable outcomes in strabismus surgery (28-33). Visual acuity, gender, age at surgery, surgical method, preoperative deviation, presence of amblyopia, duration of the exodeviation, and anisometropia have been found to affect the surgical outcome in exotropia (30). Since the relationship between strabismus and amblyopia is very complicated and each can be causal of the other (23), the same factors could be potential predictors of amblyopia development as well. Therefore, in the current study, we compared amblyopic and non-amblyopic eyes with the history of exotropia surgery in order to identify the factors associated with the postoperative development of amblyopia.

Our findings indicate that preoperative deviation is the only factor which determines the rate of amblyopia following exotropia surgery. Indeed, subjects with larger preoperative deviations had a larger chance of amblyopia development after a single surgical intervention. Other preoperative factors such as age at surgery, visual acuity, gender, strabismus type and the number of operated muscles failed to show a significant association with the postoperative development of amblyopia. Preoperative deviation has also been described as the most important parameter in determining favorable outcome in individuals whose strabismus was treated with surgery (28-30,32,34-36).

In order to investigate the factors affecting postoperative amblyopia rate we utilized Cox multivariate survival analysis. This method provides both stepwise forward multiple regression analysis and survival analysis. Unlike some previous investigations which have indicated that reoperation rates, loss of fusion and risk of developing amblyopia are greater in younger cases (37-39), our findings didn't establish a significant difference between various age groups in terms of postoperative amblyopia rate. However, a larger sample population is needed to confirm the relationship between the age of patients and the risk of amblyopia development after surgery.

In the present study, the postoperative amblyopia rate was 50%, which was higher than previous studies (5.9%-28.6% in Keenan and Willshaw (1994) (26); 1%-16% in Yam *et al*., (2012) (27); and 8%-13% in Baker *et al*. (2008) (25)). These controversial results could be attributed to the variable criteria used in defining amblyopia by different studies and to differences in methodologies. For example, Keenan and Willshaw (1994) (26) and Yam *et al*., (2012) (27) have investigated postoperative amblyopia rates in children, whereas the age of our population ranged from 4 to 63 years. Moreover, unlike our study, cases with amblyopia had been treated preoperatively in these investigations, which could decrease the postoperative rate. Besides, different surgical procedures have been utilized in these studies, and this could affect the final rate. Due to such a high rate of postoperative amblyopia, it has been suggested that amblyopia therapy must be initiated before strabismus surgery for best outcomes (40-41).

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