ORIGINAL ARTICLE

UDC: 617.7-053.2-089
DOI: 10.2298/VSP140915034A

Long-term motor and sensory outcomes after surgery for infantile esotropia

Dugoročni motorni i senzorni rezultati operacije dečje ezotropije

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Abstract

Background/Aim. Infantile esotropia (ET), entitled as congenital ET, is defined as an alternating, cross-fixational ET that occurs within the first 6 months of life. The aim of this study was to determine the long-term motor and sensory outcomes after surgical correction of patients with infantile ET. **Methods.** Medical records of 108 consecutive children who had bimedial rectus recession (BMR) initially for ET were reviewed retrospectively. The patients were divided into 3 groups: the group I, surgery before one-year old; the group II, surgery between one and two-year old; the group III, surgery after two-year old. **Results.** No significant differences were determined among the groups for preoperative mean angle of deviation and refractive error ($p > 0.05$, for both). Development rate of dissociated vertical deviation (DVD) was greater (40%) in the group I, and the relationship between the rate of DVD and the timing of the initial surgery was statistically significant ($p = 0.03$). Risk for additional surgery was significantly greater in patients with a younger mean age at initial surgery ($p = 0.01$). Although measurable stereopsis rate was higher in the group I (35%, 32.4%, 27.8%, respectively) the difference among the groups was insignificant ($p = 0.80$). **Conclusion.** Patients with ET have limited potential of high grade stereoacuity despite the early alignment of eyes. Early surgery also has potential effects for the development of both inferior oblique overaction and DVD earlier.

Key words:
esotropia; infant; child, preschool; ophthalmologic surgical procedures; treatment outcome.

Apstrakt

Uvod/Cilj. Dečja ezotropija (ET), koja se naziva i urođena ET, definiše se kao naizmenična, poprečnofiksirajuća ET koja nastaje tokom prvih šest meseci života. Cilj ove studije bio je da se utvrde dugoročni motorni i senzorni rezultati operacije mališana sa dečjom ezotropijom. **Metode.** Urađen je retrospektivni uvid u medicinsku dokumentaciju 108 ET dece sa bimedijalnom pravom recesijom (*bimedial rectus recessio* – BMR). Izvršena je podela na tri grupe: grupa I – operacija pre uzrasta od jedne godine, grupa II – operacija između jedne i dve godine i grupa III – operacija posle dve godine života. **Rezultati.** Nisu nađene značajne razlike među grupama u odnosu na preoperativni srednji ugao devijacije i refraktivnu grešku ($p > 0,05$ za oba parametra). Stopa razvoja disocijacije vertikalne devijacije (DVD) bila je viša (40%) u grupi I, a veza između stope DVD i vremena prve operacije bila je značajna ($p = 0,03$). Rizik od dodatne operacije bio je veliki kod dece prvobitno operisane u ranijem srednjem dobu ($p = 0,01$). Iako je merljiva stopa stereopsisa bila viša u grupi I (35%; 32,4%; 27.8%, redom), razlika među grupama bila je beznačajna ($p = 0,80$). **Zaključak.** Kod dece sa ET mala je mogućnost značajne oštrine steroskopskog vida i pored ranog usklađivanja očiju. Rana operacija može da ima uticaja i na razvoj oba ova poremećaja.

Ključne reči:
ezotropija; odojče; deca, predškolska; hirurgija, oftalmološka, procedure; lečenje, ishod.

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Introduction

Infantile esotropia (ET), entitled as congenital ET, is defined as an alternating, cross-fixational ET that occurs within the first 6 months of life [1]. Various abnormal sensory and motor disturbances such as asymmetric optokinetic nystagmus, abnormal stereopsis, dissociated vertical deviation (DVD), inferior oblique overaction (IOOA) and latent nystagmus can be exibited by time [2]. Although infantile ET has been classically described as a large-angle constant ET, amount of deviation may alter and accomodative component might be added in time [3]. Its aetiology has not precisely been known.

Although the most applied treatment option in infantile ET is bilateral medial rectus recession (BMR) surgery, the most beneficial timing of surgery remains controversial [4]. Infantile ET is generally associated with a poor binocular visual outcome [2]. While early (within one year) [1] and very early (within 6 months) [5] surgeries ensures better sensory results [4], delayed surgery may provide better orthophoria and keeps away multiple interventions [6, 7].

The aim of this study is to present late sensory and motor outcomes of BMR surgery for the treatment of infantile ET.

Methods

Data of 108 patients who had BMR surgery for infantile ET and were followed for at least three years at the ophthalmology department of our instutition between 1989 and 2011 were retrospectively reviewed. Approval from Institutional Review Board was obtained and the tenets of the Decleration of Helsinki was observed.

Inclusion criteria for patients consisted of constant ET of 25 prism diopters (PD) or more beginning before 6 months of age, $\leq +3.50$ diopters (D) refractive error. Exclusion criteria were: gestational age ≤ 34 weeks, congenital nystagmus, neurologic defects, developmental delay, dysmorphia, birth trauma, paralytic strabismus, and preoperatively determined development of DVD and/or IOOA.

The preoperative and follow-up ocular examinations were performed including evaluation of visual acuity, refractive error with cyclopentolate (Sikloplejin®, Abdi Ibrahim, Istanbul, Turkey), and a complete eye examination including ophthalmoscopy and ocular motility. Visual acuity (VA) was tested with a linear tumbling "E" or Snellen charts in verbal children and with the presence or absence of normal fixation in preverbal children. Pre- and postoperative angle of deviations (preoperative measurements were those immediately prior to surgery and not the deviation size at initial presentation) at near (30 cm) and distance (5 m) were measured by prism cover test with appropriate spectacle correction in primary, gaze up and gaze down positions when possible. If this was not possible, angle of deviation was measured with corneal light reflections (Hirschberg method) or Krimsky prism tests. Ductions and versions were evaluated by both observation and photographic recording. Inferior oblique muscle overaction or underaction, and DVD were examined. Stereoacuity was measured by the Titmus stereopsis test.

Surgeries were applied under general anesthesia by opening limbus-based conjunctival incision in all cases. Muscles were reattached to the sclera by using partial thickness scleral passes, and recession was measured from the original muscle insertion. Surgical dosages were determined according to standard tables [8]. Additional treatment was performed as needed for residual ET, secondary exotropia (XT), IOOA, DVD, accommodative ET, or amblyopia. Postoperative surgical success was defined as alignment within 10 PD of orthotropia at the final examination.

Patients meeting the abovementioned elegibility criteria were devided into 3 groups based on the time of the initial BMR surgery: the group I, surgery before one-year old; the group II, surgery between one and two-year old; the group III surgery after two-year old. Pre- and postoperative angle of deviation, additional extraocular muscle surgeries, the number of surgical procedures, VA, fixation preference, refraction, stereopsis, amount of the recession of the rectus muscles, development of IOOA and DVD were evaluated and the results of the three groups compared.

The normal distribution was checked using the Kolmogorov-Smirnov test. Comparisons between the groups were completed using a Pearson χ^2 test for categorical variables and a non-parametric Kruskal-Wallis test for continuous data. Non-parametric *post-hoc* tests with bonferroni correction were performed to datas which were significant with Kruskal-Wallis test. IBM SPSS Statistics for Windows Ver. 20.0 was used for the statistical analysis, and p value < 0.05 was considered significant.

Results

Pre- and postoperative data of the groups are summarized in Tables 1 and 2. Distribution of sex and mean follow-up time among the groups were similar ($p > 0.05$). There was no significant difference among the groups in refractive error or angle of deviation at the initial visit ($p > 0.05$). Visual acuity of the worse eye taken at the final examination was higher in the group III, but there was no statistically significant difference among the groups (VA of the worse eye was analyzed as a continuous variable $p = 0.06$). The mean angle of ET at the last visit after the surgery was better in the groups II and III compared to the group I ($p = 0.04$, $p < 0.001$; respectively). The mean amount of medial rectus recession was similar in all the groups ($p > 0.05$). Second-step or more surgery was performed on 65% children in the group I and 38.2% in the group II and 27.8% in the group III ($p = 0.03$). The rate of consecutive XT after surgery was higher in the group I ($p = 0.32$). Postoperatively, IOOA developed 50.9% of all cases by time and the difference between the rates of IOOA of the groups was insignificant ($p = 0.62$). However, the mean age of the patients for the development of IOOA was significanly low with respect to the other groups in the early surgery group ($p = 0.006$, $p < 0.001$; respectively). The presence of IOOA was associated with a higher rate for the development of consecutive XT ($p < 0.01$). DVD development was also higher in the group I and a significant difference was found among the groups ($p = 0.03$).

Table 1

Preoperative data of the patients

Patients	Group 1 (< 1-year-old)	Group 2 (> 1 and < 2-year-old)	Group 3 (> 2-year-old)	*p*
Number of patients (n)	20	34	54	
Gender (%)				
male	12 (60)	23 (68)	33 (61)	0.78
female	8 (40)	11 (32)	21 (39)	
Preoperative refractive error [D; mean ± SD (range)]				
spheric	1.7 ± 0.8 (0–3.25)	1.4 ± 1.3 (-3.25–3.25)	1.6 ± 1.1 (-1.00–3.25)	0.80
astigmatic	0.5 ± 0.8 (0–2.75)	0.4 ± 0.6 (-0.75–1.75)	0.5 ± 0.7 (-1.50–3.00)	0.67
Preoperative angle of deviation [PD; mean ± SD (range)]				
distance	32.7 ± 10.4 (25–70)	36.9 ± 11.5 (25–70)	34.3 ± 9.2 (25–70)	0.29
near	32.7 ± 10.4 (25–70)	37.0 ± 11.9 (25–70)	34.2 ± 8.8 (25–60)	0.36
Age at initial examination [months; mean ± SD (range)]	8.4 ± 3.5 (3–12)	15.6 ± 4.9 (8–24)	40.4 ± 22.6 (10–132)	< 0.0001* (The same for all comparisons)
Age at first surgery [months, mean ± SD (range)]	10.2 ± 2.1 (6–12)	19.6 ± 4.2 (13–24)	47.7 ± 20.9 (25–144)	< 0.0001* (The same for all comparisons)
Amount of BMR surgery [mm, mean ± SD (range)]	5.3 ± 0.3 (5–6)	5.5 ± 0.3 (5–6)	5.2 ± 0.3 (5–6)	Group 1–2 0.48 Group 1–3 0.48 Group 2–3 0.15

D – diopters; n – number; PD – prism diopters; SD – standard deviation; BMR – bimedial rectus recession.
***p* < 0.05; < *Post hoc* tests with Bonferroni correction were applied to all datas which were significant with Kruskal Wallis Test.**

Table 2

Postoperative data of the patients

Characteristics	Group I (< 1-year-old)	Group II (>1 and < 2-year-old)	Group III (> 2-year-old)	*p*
n	20	34	54	
Only BMR, [n (%)]	7 (35)	21 (61.8)	39 (72.2)	0.03*† (Significance results from Group I)
Additional surgery, [n (%)]	13 (65)	13 (38.2)	15 (27.8)	
BMR+Residual esotropia surgery	7 (35)	6 (17.6)	7 (13)	
BMR+İnferior oblique muscle surgery	1 (5)	3 (8.8)	6 (11.2)	
BMR+Consecutive exotropia surgery	4 (20)	3 (8.8)	1 (1.8)	
BMR+DVD surgery	1 (5)	1 (3)	1 (1.8)	
Number of operations [mean ± SD (range)]	1.95 ± 1.0 (1−4)	1.50 ± 0.75 (1−3)	1.35 ± 0.75 (1−5)	Group 1−2 0.24 Group 1−3 0.01* Group 2−3 0.78
Follow-up period [years, mean ± SD (range)]	7.75 ± 3.1 (3−13)	7.56 ± 4.0 (3−18)	6.87 ± 3.0 (3−16)	0.54
Refractive error at final visit [D; mean ± SD (range)]				
spheric	1.1 ± 1.2 (-1.50−3.75)	1.2 ± 2.0 (-7.00−4.75)	1.0 ± 1.2 (-1.00−5.00)	0.46
astigmatic	0.3 ± 1.6 (-4.50−3.00)	0.7 ± 1.1 (-1.75−3.25)	0.6 ± 1.0 (-2.00−4.50)	0.62
Angle of deviation at final visit [PD; mean ± SD(range)]				Group 1−2 0.04* Group 1−3 < 0.001*
distance	8.8 ± 5.0 (0−18)	5.7 ± 6.6 (0−25)	4.4 ± 5.2 (0−20)	Group 2−3 1
near	9.2 ± 5.1 (0−18)	6.7 ± 6.4 (0−20)	6.2 ± 5.4 (0−18)	0.09
Stereopsis, [n (%)]				
present	7 (35)	11 (32.4)	15 (27.8)	0.80
absent	13 (65)	23 (67.6)	39 (72.2)	
Postoperative IOOA, [n (%)]	11 (55)	19 (55.9)	25 (46.3)	0.62
Age of the development of IOOA, [months, mean ± SD (range)]	22.9 ± 11.5 (8−42)	55.3 ± 33.0 (20−131)	54.8 ± 20.1 (18−111)	Group 1−2 0.006* Group 1−3 < 0.001* Group 2−3 1
Postoperative DVD, [n (%)]	8 (40)	6 (17.6)	7 (13)	0.03* (Significance results from Group I)
Age of the development of DVD [months, mean ± SD (range)]	43.3 ± 28.3 (24−108)	90.6 ± 47.5 (50−143)	77.0 ± 41.5 (24−128)	Group 1−2 0.03* Group 1−3 0.03* Group 2−3 0.51
Consecutive exotropia at the final visit [n (%)]	5 (25)	6 (17.6)	6 (11.1)	0.32
The VA of the worse eye at the final visit [mean ± SD (range)]	0.75 ± 0.32 (0.1−1.0)	0.77 ± 0.24 (0.1−1.0)	0.85 ± 0.23 (0.2−1.0)	0.06
Success rate [n (%)]				
distance	14 (70)	27 (79.4)	48 (88.9)	0.14
near	11 (55)	25 (73.5)	42 (77.8)	0,14

D − diopters; N − number; PD − prism diopters; SD − standard deviation; IOOA − inferior oblique muscle overaction; DVD − dissociated vertical deviation; VA − visual acuity; BMR – bimedial rectus recession.
***p* < 0.05; †difference between only bimedia rectus recession (BMR) and additional surgery. *Post hoc* tests with Bonferroni correction were applied to all datas which were significant with Kruskal Wallis test.**

The mean number of reoperation was smaller in the group III compared to the group I ($p = 0.01$). Success rate (defined as deviation of ≤ 10 PD at the final examination) was higher in the group III, but it was not statistically significant ($p = 0.14$).

The number of patiens who had developed gross stereoacuity (at least 3000 seconds of arc) at the final visit was higher in the group I (median = 400 seconds of arc $p = 0.80$). No patient had high-grade (40−60 sec of arc) stereopsis within the groups. No postoperative complications were observed in any of the patients. Anterior segment and fundoscopic examination were normal in all the patients.

Discussion

The aim of the infantile ET treatment is to provide orthophoria with better binocular vision and ocular motor development. However, deficient binocular vision and maldevelopment of stereopsis are obtained [2]. Though some spontaneously recovered cases have been reported, main treatment for infantil ET is surgery [9, 10]. The proper time for surgery has been debated for decades, and there is growing evidence from clinical and animal studies describing enhanced sensory and ocular motor development after early surgery during the critical periods of development [11]. While main disadvantages of early surgery were increased risk of amblyopia and difficulty in obtaining reliable and accurate preoperative measurements, more reliable and accurate preoperative measurements were main advantages of late surgery [3]. However, a long-term study addressed that orthoptic measurement had no negative impact on long-term eye alignment in patients who had early surgery for infantile ET [12].

Although infantile ET requires surgical correction, the most beneficial timing of surgery remains controversial. According to our results, it is clear that alignment can be achieved succesfully in children with infantile ET with one surgical procedure performed after age one-year (Table 2). While 35% of the patients achieved a final ocular alignment within 10 PD with one operation in the group I, it was 52.8% of the patients who had surgery after one year of age ($p = 0.03$). Common concerns about early surgery are that the angle of deviation may have greater instability and that it may be difficult to obtain accurate measurement of the angle of deviation for surgical planning [12, 13]. In our study there was no significant differences between the early and late surgery groups in the rate of postoperative surgical success. However, the rate of additional surgical procedures for ocular alignment of the early surgery group (65%) was significantly higher with respect to other groups ($p = 0.03$). Wright et al. [14] performed additional surgery on 57% of the patients who had early surgical alignment and who were followed for 2−8 years. Birch et al. [15] did on average 1.5 surgeries on 73 patients followed 4 to 7 years and our results with a longer follow-up period (1.51 surgeries on 108 patients followed 3−18 years) were similar to those of Birch et al. Helveston et al. [1] reported 1.1 additional reoperation procedures rate per patient who had BMR surgery between 83 and 159 days of age and who were followed for 8 to 10 years. In the present study, additional operation rate *per* patient who had BMR surgery before one year of age with 3−13 years follow-up was 1.6. Thus early surgical alignment of patients with infantile ET may not assure the maintenance of alignment.

It was reported that the consecutive XT ratio was higher (38%) in patients operated before 6 months of age compared to the patients operated after 6 months of age (26%) for infantile ET. However, all the patiens were treated with 7 mm BMR surgery in that study [16]. Another factor that might have been responsible for developing consecutive XT may be larger recessions (> 6.0 mm) in the early group, but maximum recession value was 6.0 mm in our study. Larger recessions of medial rectus muscles also may have an influence on the development of adduction limitation which is also a significant risk factor for the development of consecutive XT in the long-term follow up [17]. The incidence of consecutive XT tends to increase with time and multiple surgeries are strongly correlated with a high risk of consecutive XT [18, 19]. Correspondingly, multiple surgeries were also associated with the development of consecutive XT compared to the patients (without grouping) aligned with one surgery in our study ($p = 0.002$). Twenty five percent of consecutive XT in early group seems to be high and this finding may be related with difficulty of the measurement of deviation at distance in the first year of life or long-term follow up of the present study. However, there was no statistically significant difference when compared to the other groups ($p = 0.32$). The rate of consecutive XT did not vary with the level of VA, and amblyopia was not associated for the development of the consecutive XT in the present study ($p = 0.76$).

The development of stereoacuity is correlated with several factors, including VA, ocular alignment, and intact cortical processing [2]. Stereopsis is not present at birth but starts to develop within the 3rd and 4th months of life and rapidly developes during the first 6 months of life in humans [2, 20]. Prospective studies showed that surgical alignment within the first 24 months of life is associated with better stereopsis [10], especially within the period of plasticity at 2−4 months of age for the development of stereopsis [14]. In final report of the "early *vs* late infantile strabismus surgery study" (ELISSS), cases with early surgery (between 6−24 months) had better stereopsis in comparison with the cases with delayed surgery (between 32−60 months) at a 6-year follow up [21]. However Helveston et al. [1] reported that only 4 (25%) cases had stereopsis in their 10 cases of infantile ET who had BMR surgeries within 6 months (83−159 days) of age with a long-term follow up, and they pointed out that the development of stereopsis could be increased with early surgery and stereopsis might be developed by structural factors rather than the timing of the surgery. Although duration of misalignment within the critical period has been found to be the most important factor for the development of stereoacuity in some studies, the results of the present study show that early surgical alignment is not associated with better stereoacuity outcomes. No significantly greater proportion of children in the early surgery group developed stereopsis than children in the other groups. In our study even with early surgery, only 35% of the children developed gross stereopsis (Titmus-Fly) and no one developed high-grade stereopsis (40−60 seconds of

arc). Furthermore, all children (without grouping) with any degree of stereopsis have better VA ($p = 0.03$).

DVD is the most common manifestation of the dissociated strabismus complex. Early alignment has not prevented development of dissociated strabismus [1]. The longer a patient is followed after alignment for congenital ET (up to 6 years of age), the more likely DVD is to be found [22]. In one study DVD developed in 34.8% of the cases who had undergone bimedial rectus recession [23]. Rate of DVD was 40% in the early group in the present study. When compared with the other groups this difference was statistically significant ($p = 0.03$). DVD development age was also earlier in the group I ($p = 0.03$). DVD is present in 35.3% of all patients (without grouping) who develop consecutive XT following surgical correction of infantile esotropia ($p = 0.07$). In our study, the incidence of DVD in early group was similar to other studies. However, Arslan et al. [23] reported that it may be an underestimation in the other groups due to difficulties in differential diagnosis in patients with IOOA coexisting DVD. In contrast to Arslan et al. [23] study, early surgery made more likely to have DVD development in the present study.

IOOA is commonly associated with infantile ET. In a study, IOOA was reported in 48% of the patients with infantile ET [24]. However, Eustis et al. [25] reported that development of IOOA in infantile ET was 55%. In the present study, IOOA was developed in 50.9% of all cases by time and the difference between the rates of IOOA in the groups was insignificant ($p = 0.62$). However, mean age of the patients for the development of IOOA was significanly lower in the early surgery group with respect to the other groups ($p = 0.006$ and $p < 0.001$, respectively).

This study has some limitations. The sample size was small, the study was a non-randomized retrospective clinical trial that was from a single institution with a limited number of cases and the data provided may not be representative of other medical centers in our country. In this study we excluded cases with IOOA or DVD preoperatively to determine the development rate and time of these pathologies. However these two conditions are more difficult to identify in younger patients and also tend to present later after the infantile esotropia, regardless of surgical intervention. The excluding DVD and IOOA in the groups II and III might lead to introduce a selection bias. While difficult to confirm, one would assume that many of those children in the first group would have developed DVD and IOOA if they had waited on surgery.

Conclusion

Patients with infantile ET have potential of gross stereopsis but high grade stereoacuity cannot be obtainable in the majority of them despite the early alignment of eyes. Not only the age of ocular alignment but also some constutional factors, mentioned by Helveston et al. [1], seem to have some effects on the development of binocular vision with high-grade stereo acuity in patients with infantile ET who are surgically treated. Early surgery also has potential effects for the development of both IOOA and DVD earlier. Early surgery should be performed to patients with infantile ET considering the advantages and disadvantages of this procedure. Very early surgery (< 6 months) may have better results but this study does not include such cases.

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Received on September 15, 2014.
Accepted on April 24, 2015.
Online First March, 2016.