Axial length and refraction errors in premature infants with and without retinopathy of prematurity

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Background. *Preterm children, to a greater extent, can be affected by myopia in infancy and early childhood. Refractive errors can be related to the irregular growth of the eye.*

Purpose. *To assess the incidence of refractive errors in groups of premature infants, aged 1 to 3 years, without ROP, with regressed ROP, and ROP treated with laser photocoagulation (LP).*

Material and Methods. *Ophthalmological examination findings of 175 premature infants were studied. At the age of 4-5 weeks, the children were examined for ROP. Within the period between 6 months and 3 years, the children underwent standard ophthalmological examination and ultrasound diagnosis through closed eyelids. The findings were analyzed in three groups based on the main diagnoses: group 1, children without ROP; group 2, children with spontaneously regressed ROP; group 3, children with ROP, treated with retinal laser photocoagulation of avascular zones. MedCalc v.17.4 (MedCalc Software bvba, 1993-2017) was used to statistically process the data.*

Results. *In 111 children (63%) of group 1, axial length (AL) of the right and left eyes was 19.3±1.1 mm and 19.4±1.1 mm, respectively. Hyperopia was noted in the right eye in 104 children (93.7%) and in the left eye in 105 children (94.6%). In 42 children (24%) of group 2, AL was 19.2±1.2 mm and 19.2±1.3 mm in the right and left eyes, respectively. Hyperopia was noted in the right eyes in 39 children (92.9%) and in the left eye in 37 children (88.1%). In 22 children (13%) of group 3, AL of the right and left eyes was 18.6±1.1 mm and 18.8±1.2 мм, respectively. Myopia was noted in the right eye in 6 children (27.3%) and in the left eye 3 children (13.6%); hyperopia was noted in the right eye in 11 children (50%) and in the left eye in 12 children (54.6%); emmetropia was in the right eye in 1 child (4.5%) and in the left eye in 2 children (9,1%); and astigmatism was in the right eyes in 4 children (18.2%) and in the left eye in 5children (22.7%).*

Conclusions. *It was found that axial length in preterm children at the age of 1-3 years with a history of LP for ROP was smaller than that in children without ROP and with regressed ROP (18.7 mm versus 19.35 mm and 19.2 mm, respectively). The incidence rates of myopia (20.45%) and astigmatism (20.45%) were higher in preterm children with LP-treated ROP as compared to children without ROP (4.95% and 2.7%, respectively) and with regressed ROP (8.3% and 1.2%, respectively).*

Keywords:
axial length, retinopathy of prematurity

Background

Retinopathy of prematurity (ROP) is one of the leading causes of bilateral blindness and visual impairment in premature infants in the world (CRYO-ROP trial 1990), which is not always related to previous disease-associated alterations [3]. Patients with favorable treatment outcome are also at high risk of ophthalmic pathology. Among eye diseases, myopia has a special place [9]. The Multicenter Study of the Early Treatment for Retinopathy of Prematurity (ETROP) has shown that 60% of patients, who had undergone early laser photocoagulation, developed visual acuity worse than 20/40 and 29% of patients had unfavorable outcomes (visual acuity worse than 20/200) [10].

Premature infants, to a greater extent, can be affected by myopia in early infancy and early childhood, opposite to full-term newborns, for whom hypermetropic refraction is common. In 1992, Quinn and colleagues showed that, in 20 % of premature infants with birth weights of less than 1251 g and with a self-regressing form of ROP, myopia developed within the first two years of life; high myopia (> 5.0 D) was observed in 4.6% [16].

It is crucial to understand the mechanism of refractive error development and progression in premature infants with ROP for searching for new treatment approaches and consulting parents on the further course of the disease. Today, researchers associate myopia with prematurity, ROP, and laser photocoagulation sequelae [6, 18].

However, the major cause of development and progression of a refractive error is still unclear [3, 15]. Therefore, to determine the cause of myopia it is necessary to identify the changes in a biometric profile of premature infants' eyes in early infancy and early childhood.

The purpose of the present paper was to assess the incidence of refractive errors in groups of premature infants, aged 1 to 3 years, without ROP, with self-regressive ROP, and ROP treated with laser photocoagulation (LP).

Material and Methods

Ophthalmological examination findings of 175 premature infants were studied. The study was carried out on the basis of Policlinic of SI "The Filatov Institute of Eye Diseases and Tissue Therapy". Over stipulated time periods, all infants were examined for ROP at Department of Prematurity Pathology and Department of Neonatal Reanimation and Intensive Therapy. The stage and severity of ROP, if occurred, was classified according to the International Classification of ROP (ICROP, 2005) [11]. The infants with scarring Stages 4 and 5 were excluded from the study. Within the period between 6 months and 3 years, the children underwent standard ophthalmological examination which included physical examination, visual acuity testing, tests for strabismus, assessment of eyeball movements and convergence, wet retinoscopy for clinical refraction (double instillations of 0.5% cyclopentolate), ultrasound scanning, fundus ophthalmoscopy, and ultrasound biometry.

Axial length (AL) was measured during the outpatient examination. The findings were analyzed in three groups based on the main diagnose: group 1, children without ROP; group 2, children with spontaneously regressed ROP; group 3, children with ROP, treated with retinal laser photocoagulation of avascular zones.

MedCalc v.17.4 (MedCalc Software bvba, 1993-2017) was used to statistically process the data [1,13].

In analysis of qualitative attributes, the results are given as percentage values and their standard errors (±m%). Scheffe's Test for multiple comparisons was used to reveal statistical differences between means in normally distributed data.

Results

Based on ophthalmic examination, 175 children were divided as follows: group 1, 111 children (63%) without ROP; group 2, 42 children (24%) with simultaneously regressed ROP; and group 3, 22 children (13%) with ROP treated with LP.

At the first study phase, we measured AL in the premature infants, aged 6 months to 3 years, in the three groups. A statistically significant difference was revealed in the AL values in group 3 compared to values in groups 1 and 2 ($p=0.04$). Table 1 demonstrates Scheffe's test data on the AL values. The mean value and 95% CI are given for right and left eyes.

At the second study phase, we distributed the children according to diagnosis in the right and left eyes in the three groups. Tables 2 and 3 demonstrate that refraction-based distribution in group 3 statistically significantly differed from that in groups 1 and 2 ($p<0.001$).

Table 2 demonstrates that, in the right eye, hyperopia was diagnosed in 93.7% and 92.9% of the infants in groups 1 and 2, respectively, while, in group 3, hyperopia was found in 50% while 27.3% and 18.2% of the infants had myopia and astigmatism, respectively.

Table 3 shows that, in the left eye, hyperopia was diagnosed in 94.6% and 88.1% of the children in groups 1 and 2, respectively, while, in group 3, hyperopia was found in 54.6% while 13.6% and 22.7% of the children had myopia and astigmatism, respectively.

Discussion

Our paper was a study of a biometric parameter, in particular, axial length of premature infants without ROP, with regressed ROP, ROP treated by laser photocoagulation. It does not provide proof but shows the mean axial length. It is a well-known fact that preterm children have higher rates of myopia as early as in early childhood; and this is, in a greater extend, true for children with a history of laser treatment for retinopathy of prematurity [3, 15]. Since "the third epidemic" has been declared in developing countries, including Ukraine, it is expected that the incidence of refractive errors, and, first of all, myopia, will increase in children [9]. In this regards, early diagnosis of refraction errors is an important predictor to avoid refractive amblyopia which can develop in these patients [18].

During the first 3-12 months of life, an eye is in the process of achieving emmetropia [19]. Thus, by the age of 1 year, there can be certain changes in the anatomical ocular structures. It is known that major causes of myopia in children are long axial length of the eye, shallower anterior chamber, and thicker lenses [14, 5]. However, which of those is more influential in myopia development in preterm babies is still unclear. Various hypotheses have been suggested. Congenital myopia has been associated with an abnormal diameter of the cornea and steep curvature, shallow anterior chamber, higher axial length, and thicker lens (Fledelius 1976; Gordon & Donzis 1986; Quinn et al., 1992). Thereafter, new evidence on the anatomical features of ocular tissues in the premature infants has come to light telling that such children are characterized by the convex cornea, deeper anterior chamber, thicker lens, and shorter axial length. These anatomical features are associated with irregular growth [4, 7, 8, 17].

In our study we assessed only axial length of the eye since this diagnostic procedure is performed to children aged 6 months to 3 years through closed eyelids. According to the data obtained, AL in premature infants with a history of LP for ROP was smaller than that in children without ROP and with regressed ROP ($p=0.04$). The rates of refractive errors in the children with a history of LP for ROP significantly differed from those in groups 1 and 2. It should be noted that this regularity was noted in early infancy and early childhood. In this cohort, the myopia and astigmatism rates were 20.45% and 20.45%, respectively.

The issue what exactly determines the refractive abnormality in preterm patients with ROP still is a subject of discussion [2, 3, 20]. We endorse a view that laser treatment over the whole circumference of the retina (360°) possibly hampers ocular growth, and, consequently, results in a shorter AL even in the presence of myopia [12]. In addition, there is stunted growth of the posterior eye and active growth of the anterior eye. Chang-Sue Yang et al. performed a prospective, cross-sectional study on ocular structures in preterm children at the age of 9 years. They found some structural peculiarities including thicker lens (3.94 versus 3.39 mm in full-term children) and shallower anterior chamber depth (2.91 versus 3.58 mm). Also, the authors demonstrated that the eyes with laser-treated ROP had greater vertical corneal radius (7.67 versus 7.47 mm), smaller vertical corneal radius and the mean corneal curvature was steeper in eyes with laser-treated ROP when compared to full-term controls. (7.73 versus 7.76 mm). However, no difference in terms of axial length between the two groups was noted (23.32 versus 23.24 mm) [3].

We carried out, for the first time, the analysis of axial length in premature children at the age of 1 to 3 years. The analysis data showed the difference in axial length between children without ROP, regressed ROP, and LP-treated ROP ((18.7 mm versus 19.35 mm versus 19.2 mm, respectively). These findings can give evidence of importance of a refractive component and, consequently, development of refractive myopia and astigmatism. That is why it is required to perform a major and detailed study of all anatomical ocular structures in early and late childhood.

In conclusion, firstly, it was found that axial length in preterm children at age of 1-3 years with a history of LP for ROP was smaller than that in children without ROP and with regressed ROP (18.7 mm versus 19.35 mm and 19.2 mm, respectively). Secondly, the incidence rates of myopia (20.45%) and astigmatism (20.45%) were higher in preterm children with LP-treated ROP as compared to children without ROP (4.95% and 2.7%, respectively) and with regressed ROP (8.3% and 1.2%, respectively).

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Table 1. Scheffe's Test data on axial length in the three groups

Parameter studied	$\overline{X}$ ±SD			Level of significance of differences, p
	Group 1	Group 2	Group 3	
Axial length of the right eye	19.3±1.1	19.2±1.2	18.6±1.1*	0.04
Axial length of the left eye	19.4±1.1	19.2±1.3	18.8±1.2	0.07

Note: * – difference from group 1 is statistically significant (Scheffe's criterium) p<0.05.

Table 2. Refraction-based distribution of the children in three groups, the right eye

Refraction in the right eye	Groups						Level of significance of differences, p
	Group 1		Group 2		Group 3		
	n	%	n	%	n	%	
Myopia	4	3.6	3	7.1	6	27.3	<0.001
Hyperopia	104	93..7	39	92.9	11	50	
Emmetropia	0	0	0	0	1	4.5	
Astigmatism	3	2.7	0	0	4	18.2	

Note: * - Refraction-based distribution in group 3 differs from that in groups 1 and 2 (p<0.001)

Table 3. Refraction-based distribution of the children in three groups, the left eye

Refraction in the left eye	Groups						Level of significance of differences, p
	Group 1		Group 2		Group 3		
	n.	%	n	%	n	%	
Myopia	3	2,7	4	9.5	3	13.6	<0.001
Hyperopia	105	94.6	37	88.1	12	54,6	
Emmetropia	0	0	0	0	2	9.1	
Astigmatism	3	2.7	1	2.4	5	22.7	

Note: * - Refraction-based distribution in group 3 differs from that in groups 1 and 2 (p<0.001)

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