Retinopathy of prematurity: refractive errors in patients treated with cryotherapy or laser

Retinopatia da prematuridade: achados refrativos pós-tratamento com crioterapia ou laser

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SUMMARY

Purpose: **To examine the spherical equivalent of refractive errors in preterm children with threshold retinopathy of prematurity treated with cryotherapy or laser.**

Patients and Method: **A group of 14 one-year-old children (selected from 761 preterm children born at the Hospital São Paulo of the Universidade Federal de São Paulo between 1988 and 1998) with stage 3 threshold retinopathy of prematurity treated with cryotherapy or laser photocoagulation was enrolled in the study and the spherical equivalent under cycloplegia was analyzed. Statistical analysis of the results was performed using Wilcoxon and Mann-Whitney tests.**

Results: **64.3% of the patients developed myopia. Of the patients who were treated with cryotherapy 80% showed high myopia and 20% low hyperopia. The mean of the spherical equivalent was –3.10 D in the right and –3.25 D in the left eye. There was no statistically significant difference between the two eyes regarding the refractive outcome. Concerning patients treated with laser, 55.6% showed myopia of which 20% was high myopia and 80% low myopia; 11.1% showed no refractive error and 33.3% developed low hyperopia. The mean of the spherical equivalent was –0.58 D in the right eye and -0.83 D in the left eye. A statistically significant diference was found between the two eyes. The correlation of refractive results in both groups of patients showed an increase in the amount of high degree myopia in patients treated with cryotherapy ($P<0.05$).**

Conclusions: **Myopia is a frequent finding in children treated for retinopathy of prematurity. Myopia not only is more frequent but it appears with higher degrees in children treated with cryotherapy as compared with those treated with laser.**

Keywords: Retinopathy; Prematurity; Cryotherapy; Laser.

INTRODUCTION

Retinopathy of prematurity is a vascular disease related to retinal blood vessel formation affecting preterm newborns and its severity presents an inversely proportional relation to gestational age and weight at birth [1, 2].

At present, advances in neonatology allow survival of children with extremely low gestational age and weight at birth, leading to an increase in the number of patients with ocular alteration[3], especially retinopathy of prematurity.

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Tablel 1. Characteristics of the studied population

Patient No.	Sex	Gestational Age (Weeks)	Weight at Birth (grams)	Severity of Retinopathy	Performed Treatment
28	F	0.26	850	3 - Plus	Cryo
151	M	30	1070	3 - Plus	Cryo
226	M	28	710	3 - Plus	Cryo
357	M	26	750	3 - Plus	Cryo
409*	F	26	820	3 - Plus	Cryo
481	M	29	840	3 - Plus	Cryo
589	M	30	1600	3 - Plus	Laser
598	M	27	1100	3 - Plus	Laser
607	M	28	850	3 - Plus	Laser
638	F	33	1420	3 - Plus	Laser
643	M	29	1070	3 - Plus	Laser
651	F	30	890	3 - Plus	Laser
685	M	25	705	3 - Plus	Laser
703	F	26	680	3 - Plus	Laser
746	F	26	590	3 - Plus	Laser

*Death before one year of age

Different authors [3-8] reported a higher predisposition to ametropia, specially myopia, in children who presented retinopathy of prematurity. Differences in the refractive value according to the severity of retinopathy [5] and to the type of performed treatment, cryotherapy or lasertherapy, were also found [7, 8].

The purpose of this study is:

-To determine the refractive characteristics of a population consisting of preterm children born at the Hospital São Paulo, Escola Paulista de Medicina - Universidade Federal de São Paulo, who presented retinopathy of prematurity and were submitted to treatment;

-To compare the type of refractive error with the used method (cryotherapy or lasertherapy).

PATIENTS AND METHODS

The charts of 761 preterm children, born at the Hospital São Paulo of the Universidade Federal de São Paulo - Escola Paulista de Medicina in the period between January 1988 and April 1988 and followed-up at the Retina and Vitreous Sector, were retrospectively analyzed.

Of all followed-up children, 15 developed retinopathy of prematurity requiring treatment. This group of patients was divided into two subgroups according to the received treatment. One female patient treated with cryotherapy died at the age of 4 months and, therefore, was excluded from the study. The remaining 14 patients continued follow-up, 5 in the cryotherapy subgroup and 9 in the lasertherapy subgroup (Tables 1, 2).

Indication of treatment was according to the criteria of the Cryotherapy for Retinopathy of Prematurity Cooperative Group [9]; the method was randomly chosen and was performed under general anesthesia in all patients.

All patients were submitted to refraction under cycloplegia using retinoscope and skiascopy bar after the age of one year. The spherical equivalent was used for this study.

Myopia was defined as <0 D and subdivided into "mild" myopia (between 0 and 3.00 D) and "high" myopia (myopia with values above 3.00 D).

Hypermetropia was defined as >0 D; up to +3.00 D, mild hypermetropia.

For the categorization of the morphological features of the fundus, the classification established by the Committee for the Classification of Retinopathy of Prematurity [10] was used, which defines *stage 3*: extraretinal fibrovascular proliferation; *plus disease*: vascular dilatation and tortuosity, pupillary rigidity or vitreous turbidity; *threshold disease*: five or more cumulative hours of stage 3 retinopahty of prematurity in zone I or II and in the presence of plus disease [11].

The Wilcoxon and Mann-Whitney tests were used for the statistical analysis of the results.

RESULTS

Of the original population of 761 preterm children born at the Hospital São Paulo and followed-up at the Retina and

Table 2. Mean of gestational age and weight at birth in the two groups of treatment

	Cryotherapy	Laser
Total number of patients	6	9
Females	2	4
Males	4	5
Mean of gestational age (weeks)	27.5	28.2
Mean of weight at birth (grams)	840	989.4

Vitreous Sector of the Escola Paulista de Medicina, 132 (17.35%) had some degree of retinopathy.

Of the 132 patients with retinal lesions, 15 (11.36%) developed stage 3 retinopathy of prematurity with "threshold disease" characteristics and were submitted to treatment. Of these 15 patients, 6 (40%) were females, 9 (60%) males; gestational age was between 25 and 33 weeks (mean 27.9 weeks); weight at birth was between 590 and 1600 grams (mean 929.7 grams).

The sample was divided into 2 groups, according to the received treatment. The cryotherapy subgroup consisted of 6 patients (2 females, 4 males) with gestational age between 26 and 30 weeks (mean 27.5 weeks) and weight at birth between 710 and 1070 grams (mean 840 grams). The lasertherapy subgroup, consisting of 9 patients (4 females, 5 males), presented a gestational age between 25 and 33 weeks (mean 28.2 weeks) and weight at birth between 590 and 1600 grams (mean 989.4 grams) (Table 2).

Refraction was performed in 10 eyes of patients treated with cryotherapy and in 18 eyes of the 9 patients submitted to lasertherapy. Of all patients, 9 (64.3%) developed myopia-like refractive error.

Of the 5 patients treated with cryotherapy, 4 presented myopia considered to be high in our study (myopia of values above 3.00 D), corresponding to 80% of these patients; 1 patient showed mild hypermetropia (less than +3.00 D), corresponding to 20%.

Considering separately the right and left eye, the spherical equivalent of the right eye ranged from +1.00 to -5.00 D (mean -3.10 D). In the left eye it ranged from +1.25 D to -5.25 D (mean - 3.25 D). Applying Wilcoxon's test to this data it was shown that there was no statistically significant difference between both eyes.

Of the 9 patients treated with diode laser, 5 (55.6%) presented myopia, which was considered high (myopia values above 3.00 D) in 1 of them (20%); in 4 patients (80%) the spherical equivalent ranged from -0.25 D to -3.00 D (mild myopia); 1 patient had no ametropia (AO plane) and 3 patients (33.3%) showed mild hypermetropia (< +3.00 D). The refractive spherical equivalent ranged from -6.00 D to +2.50 D in both eyes with a mean of -0.58 D in the right eye and -0.83 D in the left (a statistically significant difference between both eyes). The spherical equivalent value of the patients is shown in Table 3.

On comparison of the refractive results between the two groups of patients (cryotherapy and lasertherapy) a different incidence of myopia, which was more severe in the group treated with cryotherapy, can be observed (P<0.05).

Table 3. Spherical equivalent in diopters, according to performed treatment

Cryotherapy			Laser		
Patient No.	OD	OS	Patient No.	OD	OS
28	-5.00	-5.25	589	+1.50	+0.75
151	-4.00	-4.00	598	-6.00	-6.00
226	-4.00	-4.00	607	Plane	Plane
357	-3.50	-4.25	638	+2.00	+2.00
481	+1.00	+1.25	643	+2.50	+2.50
			651	-3.00	-3.00
			685	-1.50	-2.00
			703	-0.25	-1.00
			746	-0.50	-0.75
Mean	-3.10	-3.25	Mean	-0.58	-0.83

DISCUSSION AND CONCLUSION

The value of cryotherapy as treatment for retinopathy of prematurity has already been confirmed [9, 12]. Laser has been used for a long time in the treatment of retinopathy [13, 14] and its use has recently become very popular.

It is known that frequency of myopia in preterm newborns without retinopathy of prematurity is higher than in the at term population [15] and that the eyes of those patients present some specific anatomical characteristics which might contribute to myopia, such as corneal curvature increase, narrow anterior chamber, lens thickness increase with increase in refractive power [16] and smaller anteroposterior eyeball diameter than that expected for the diopter value [17].

In preterm newborns with retinopathy of prematurity the risk for myopia is even higher, but has only statistical significance in the more severe ROP cases (from stage 3 on) [18]. In these cases there is also evidence of alterations in the development of the anterior segment: microcornea, corneal curvature and lens increase [16, 19]. The fact that preterm children with retinopathy present a greater disposition to myopia-like refractive errors [3-8] was again confirmed in this study and, considering the degree of myopia according to the performed treatment, we deem that the risk for severe myopia is higher in those patients who received cryotherapy than in those treated with lasertherapy, similarly to the data found in the world literature [6, 15, 19].

There are still controversial conclusions regarding the visual prognosis of the patients with retinopathy of prematurity treated with lasertherapy or cryotherapy [6, 15]. Some studies showed that visual results are better in patients treated with laser [7,15] and a hypothesis for these results would be induction of lower myopia degrees.

Regarding myopia etiology, some authors refer to the larger tissue destroying effect of transscleral cryotherapy due to the greater and more confluent applications [7] which would lead to greater ocular wall growth; others think that it would stem from lens alterations.

Although the association of prematurity with retinopathy of prematurity and myopia is well-known, the patho-physiological mechanisms of production of this alteration remain to be clarified. In this study, the severity of the fundoscopic alterations was the same in all children and the only different characteristic between them was the received treatment. Further studies are needed to establish if the

myopia is of axial index and which is the role of cryotherapy in the development of this refractive error that constitutes an important cause of visual alteration in preterm children.

RESUMO

Objetivos**:** *Determinar e comparar as características refrativas de uma população composta de crianças pré-termo com retinopatia da prematuridade que necessitaram de tratamento com crioterapia ou laserterapia.*

Método: *Análise dos resultados da refração estática de 14 pacientes (de um total de 761 fichas de crianças) que nasceram no Hospital São Paulo da Universidade Federal de São Paulo-Escola Paulista de Medicina, entre janeiro de 1988 e abril de 1998, que completaram um ano de idade e que apresentaram retinopatia da prematuridade grau 3 com características de "doença limiar" sendo tratadas com crioterapia ou laser-terapia. Foram utilizados os testes estatísticos de Wilcoxon e Mann-Whitney para a avaliação dos resultados.*

Resultados: *64,3% dos pacientes apresentaram miopia. No grupo de pacientes que receberam tratamento com crioterapia, 80% mostrou miopia, que em todos os casos foi alta; 20% hipermetropia leve, com uma média para o equivalente esférico de –3,10D no olho direito e –3,25D no olho esquerdo (diferença entre ambos os olhos estatisticamente não-significante). No grupo de laserterapia, 55,6% mostrou miopia, sendo 20% dos casos miopia alta e 80% miopia leve; 11,1% apresentou-se sem ametropia e 33,3% com hipermetropia leve. O valor da média para o equivalente esférico foi –0,58D no olho direito e –0,83D no olho esquerdo (diferença entre ambos os olhos estatisticamente significante). A comparação dos resultados refracionais dos dois grupos mostrou uma maior incidência para miopia alta no grupo de pacientes que receberam tratamento com crioterapia (P< 0,05).*

Conclusão**:** *Existe predisposição a erros refrativos de tipo miopia nas crianças com retinopatia da prematuridade que recebem tratamento. A possibilidade de miopia grave é maior naquelas crianças tratadas com crioterapia do que nas tratadas com laserterapia.*

Palavras-chave**:** *Retinopatia; Prematuridade; Crioterapia; Laser.*

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