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Comparison of treatment results for retinopathy of prematurity by diode laser photocoagulation and cryotherapy – four years of observation

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Background: The aim of the study was to compare functional and structural outcomes of treatment for retinopathy of prematurity with diode laser photocoagulation and cryotherapy.

Materials and methods: We examined 111 children aged 4 years, treated for retinopathy of prematurity by transpupillary diode laser photocoagulation or cryotherapy. Both functional (visual acuity, orthoptic status) and structural (anterior segment and fundus examination) results were evaluated. Cycloplegic refraction was examined in all cases.

Results: Favorable functional results occurred in 87.8% of eyes in patients after cryotherapy and in 97.4% of eyes in patients after diode laser photocoagulation. Structural outcome was favorable in 87.8% of eyes treated with cryotherapy and in 96.6% of eyes treated with diode laser photocoagulation.

Conclusion: Diode laser photocoagulation is an optimal method of treatment for active stages of retinopathy of prematurity.

Key words: retinopathy of prematurity, diode laser photocoagulation, cryotherapy

INTRODUCTION

Retinopathy of prematurity (ROP) is an important cause of preventable blindness in children (1). The optimal treatment of active stage of ROP may decrease the number of blind and visually handicapped children.

The commonly used methods in ROP treatment are cryotherapy and diode laser photocoagulation. Cryotherapy is an effective treatment modality for the threshold stage of ROP (1). However, it is associated with complications like bradycardia, apneic episodes, postoperative chemosis, eyelid edema, and destruction of conjunctiva and sclera (2). According to the literature, these complications occur less commonly after diode laser photocoagulation (2). Also, the visibility of laser spots is an advantage of the latter method. It may prevent the secondary coagulation of retina which can happen during cryotherapy (3).

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The aim of the study was to compare the functional and structural results of treatment for ROP with diode laser photocoagulation and cryotherapy in children aged 4 years.

MATERIALS AND METHODS

We examined 222 eyes of 111 premature children: 61 (54.9%) girls and 50 (45.1%) boys; 53 children born between 1996 and 1999 were treated by cryotherapy (group I), and 58 children born between 2000 and 2003 were treated by diode laser photocoagulation (group II). We analyzed birth weight, gestational age and Apgar scale in all cases (Table 1).

Table 1. **Baseline characteristics of the patients**

	Group I	Group II
Birth weight (g)	600–1820 (mean, 968)	450–2000 (mean, 994)
Gestational age (weeks)	24–32 (mean, 27)	24–35 (mean, 27.8)
Apgar scale	1–9 (mean, 4)	1–10 (mean, 5)

The ROP stage was classified according to CRYO-ROP classification, taking into account the location and number of clock hours of involved retina and presence of "plus disease" (1).

Cryotherapy was performed in 98 eyes (92.4%) in threshold stage, in six eyes (5.7%) in pre-threshold stage and in two eyes (1.9%) in stage 4a of ROP (Fig. 1).

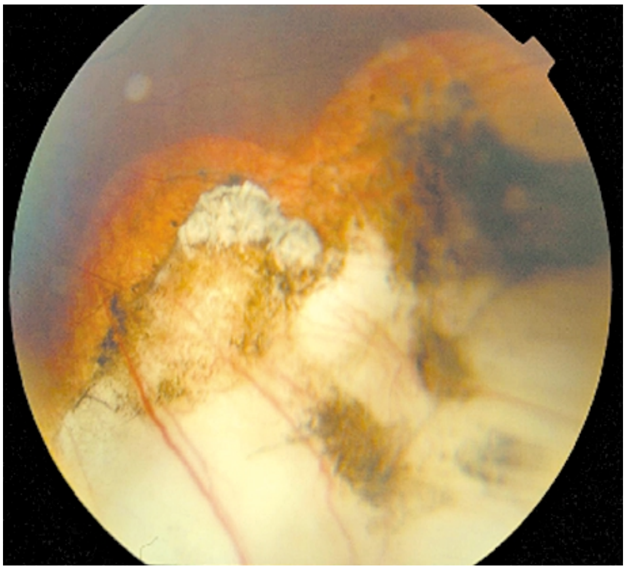

Fig. 1. Pigmented retinal scars after cryotherapy for ROP

Diode laser photocoagulation was performed in 101 eyes (87%) in threshold stage, in 11 eyes (9.5%) in pre-threshold stage and in four eyes (3.5%) in stage 4a of ROP (Fig. 2).

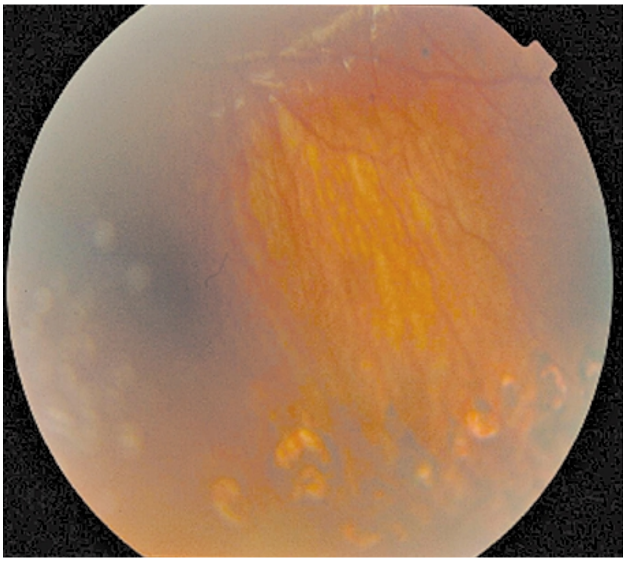

Fig. 2. Pigmented retinal scars after diode laser photocoagulation for ROP

In eyes with pre-threshold stage in both groups the lesions were located in zone 1 or in zone 2 close to zone 1. In group I, in cases with threshold stage ROP was located in zone 1 in 12 cases (11.3%) and in zone 2 or 3 in the rest of the cases. In group II, in cases with threshold stage ROP was found in zone 1 in 19 cases (18.8%) and in zone 2 or 3 in the rest of the cases. The children's age at the time of treatment was 4–18 weeks (mean, 10 weeks) in group I and 6–12 weeks (mean, 8.5 weeks) in group II. In all 4-year-old children we analyzed the functional (visual acuity using Snellen chart or Teller Acuity Charts, if needed, and orthoptic status) and structural effects (anterior segment findings and fundus examination) as well as cycloplegic refraction (using 1% tropicamide). According to CRYO-ROP classification, we defined a favorable functional result as a Snellen visual acuity better than 0.1; eyes with visual acuity scores of 0.1 or worse were classified as unfavorable (1). The structural results were considered unfavorable when one of the three signs occurred: retinal fold involving macula, retinal detachment in zone 1 or retrolental tissue or "mass" obscuring the view of the posterior pole [1].

Spherical equivalents were calculated in all cases. High myopia was defined as a spherical equivalent equal to or less than –6 D. To assess the orthoptic status we analyzed the angle of strabismus, the presence or lack of binocular vision (simultaneous perception, fusion, stereoscopic vision) as well as the presence of nystagmus. To compare the results we used the χ^2 test. All parents gave their informed consent allowing the children to participate in the study.

RESULTS

In group I we found favorable visual acuity in 96 eyes (87.8%) and unfavorable in 13 eyes (12.2%). In group II favorable function occurred in 113 eyes (98.4%) and unfavorable only in 3 cases (2.6%). The differences between the groups were statistically significant (χ^2 test, $p = 0.04$).

In group I, very good visual acuity (between 1.0 and 0.8) was present in 45 eyes (42.5%), good (between 0.7 and 0.5) in 27 eyes (25.5%). 21 eyes (19.8%) had visual acuity between 0.4 and >0.1, and the remaining 13 eyes (12.2%) – equal or less than 0.1 (unfavorable) (Fig. 3).

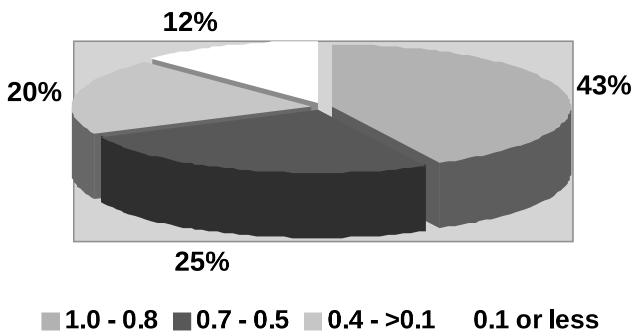

Fig. 3. Visual acuity in group I

In group II 83 eyes (71.6%) had a very good and 20 eyes (17.2%) – good visual acuity. In 10 cases (8.6%) we found visual acuity between 0.4 and >0.1, and the

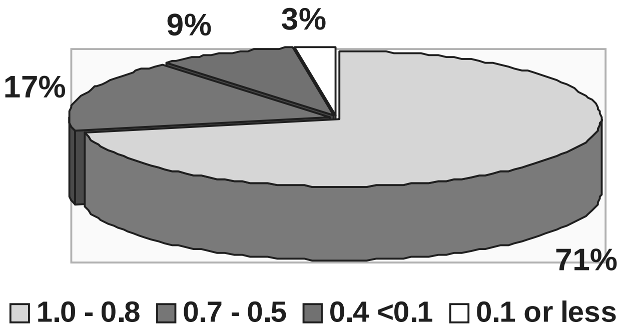

Fig. 4. Visual acuity in group II

remaining three (2.6%) had unfavorable function (equal or less than 0.1) (Fig. 4).

In group I 59 eyes (55.7%) were myopic, 31 eyes (29.3%) hyperopic and 4 (3.7%) emmetropic. In 12 cases (11.3%) it was impossible to measure the refractive error because of total retinal detachment. In group II, 59 eyes (50.5%) were myopic, 31 eyes (26.7%) hyperopic and 33 (19.8%) emmetropic. The refractive error was not measured in three cases (2.6%). The difference between the number of emmetropic eyes in both groups was statistically significant (χ^2 test, p = 0.0002). The distribution of spherical equivalents of refractive errors in both groups is presented in Table 2.

Table 2. **Spherical equivalent of refractive error in both groups**

Spherical equivalent	Group I (number/%)	Group II (number/%)
Myopia ≤ 3.0 D	17 / 16	28 / 24.1
Myopia > 3.0D - < 6.0D	22 / 20.8	14 / 12.1
Myopia ≥ 6.0D	20 / 18.9	17 / 14.7
Emmetropia	4 / 3.7	23 / 19.8
Hyperopia ≤ 3.0D	25 / 23.6	29 / 25
Hyperopia > 3.0D	6 / 5.7	2 / 1.7
Not measured	12 / 11.3	3 / 2.6

Astigmatism >1.0 D was diagnosed in 15 eyes (14.2%) in group I and in 20 eyes (17.2%) in group II. The values are not statistically significant (χ^2 test, p = 0.08).

Anisometropia larger than 2.0 D occurred in 8 cases (15%) in group I and in 6 cases (10.3%) in group II.

The percentage of nystagmus was higher in group I (3 cases, 5.7%) than in group II (2 cases, 3.4%).

Four children (6.9%) from group II were found to have strabismus *versus* 13 children (24.5%) from group I. The values are statistically significant (χ^2 test, p = 0.001). It was convergent strabismus in all four cases in group II and in 11 in group I. Divergent strabismus was diagnosed only in two cases in group I.

Binocular vision in group I was present in 24 cases (45.3%), absent in 18 cases (33.7%) and not assessed in 11 cases (21%). In group II binocular vision was present in 30 cases (51.7%), absent in 12 cases (20.7%) and not assessed in 16 cases (27.4%). These values are not statistically significant.

In group I, favorable structural result occurred in 93 eyes (87.8%) and unfavorable in 13 eyes (12.2%). In group II favorable structural result was present in 112 eyes (96.6%) and unfavorable in 3 eyes (3.4%). These values are statistically significant (χ^2 test, p = 0.045).

In group II, cataract occurred in one eye (0.86%). There were no other complications in the anterior segment of eyes in both groups.

DISCUSSION

The multicenter study of cryotherapy for ROP (CRYO-ROP) demonstrated cryotherapy as an effective treatment for preventing ROP progression (1). However, cryotherapy may be associated with significant systemic and ocular complications. Also, the placement of cryotherapy in the posterior zone 2 or 1 can be technically difficult and often necessitates conjunctival incision for probe placement (4). Transpupillary diode laser photocoagulation has been demonstrated to be an equally or even more effective treatment method for ROP in different studies (5, 6). For these reasons, laser photocoagulation has largely replaced cryotherapy as the preferred method of peripheral retinal ablation in infants with threshold ROP (3, 4). According to literature, it is associated with better functional and structural outcomes and a smaller number of complications (7). Passe et al. have found favorable structural results in 87.5% of eyes after diode laser photocoagulation (3). Foroozan et al. (8) described favorable structural results in 91% of cases regardless of location of ROP lesions. Steinmetz et al. (9) reported favorable structural results in 96% of treated eyes. Also, in our previous report regarding structural results in premature infants with ROP treated by diode laser photocoagulation, the favorable structural outcome occurred in 96.5% of eyes in the 12th month of life (10). McGregor et al. (5) found 15%, Hautz et al. 4.3% (11) of retinal detachment in their patients after laser photocoagulation. Hunter et al. described 6% of unfavorable structural outcomes after laser treatment (12).

In our present study, the unfavorable structural result occurred in 12% of eyes treated by cryopexy. The Cryotherapy for ROP Cooperative Group reported 25.7% of unfavorable structural results after cryotherapy (1).

Favorable functional results were present in our study in 98% of eyes after laser treatment and in 87.8% of eyes after cryotherapy. In a multicenter trial of cryotherapy for ROP there were 65% favorable and 35% unfavorable functional results (1). Axer-Siegel et al. reported better functional and structural outcomes after laser treatment for ROP in zone 1 or 2 comparing with cryotherapy (13).

Myopic refractive error occurred in our patients in about 50% of eyes regardless of the method of treatment. However, there were more emmetropic eyes and a lower incidence of high myopia in the group after laser treatment versus cryocoagulation. The Cryotherapy for

ROP Cooperative Group reported 33.3% of eyes with high myopia in children after cryotherapy (1).

The number of eyes with astigmatism higher than 1.0 D was similar in both groups in our study. The incidence of anisometropia was more common in children after cryotherapy. Similar observations were presented by Laws et al. (14).

Strabismus was more common (statistically significant values) in the group treated by cryotherapy. We have also found a higher number of patients with nystagmus after cryotherapy in our group.

According to the literature, diode laser treatment can be associated with complications in the anterior segment of the eye. In our study, we found only one eye with cataract after diode laser photocoagulation.

CONCLUSIONS

The methods of treatment for active stages of ROP have changed over the past years. Diode laser photocoagulation is an effective method in the prevention of ROP progression. The functional and structural outcomes of treatment are favorable and the number of complications is lower in comparison with cryocoagulation. Although cryotherapy remains a satisfactory therapeutic option, transpupillary diode laser photocoagulation has become the standard and the treatment of choice.

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