

Retinopathy of Prematurity: An Evaluation in the Keelung Area of Taiwan over A 10-Year Period

Ko-Jen Yang, MD; Chen-Hsin Tsai, MD; Chi-Chun Lai, MD; Chia-Shun Lu,¹ MD;
Tun-Lu Chen, MD

Background: We report on the experience of retinopathy of prematurity (ROP) at Chang Gung Memorial Hospital (CGMH), Keelung, Taiwan over a 10-year period.

Methods: A retrospective review was made of data of all premature infants with a diagnosis of ROP at Keelung CGMH between 1994 and 2003. Data on certain characteristics including gender, gestational age (GA), birth body weight (BBW), stage of ROP, and treatment modalities were collected and analyzed.

Results: Among the 458 infants screened for ROP, 148 eyes of 74 premature infants were diagnosed as having ROP. Threshold ROP occurred in 24 eyes of 12 infants. The average BBW and GA were significantly lower in the threshold than in the non-threshold ROP group ($p < 0.05$). According to medical records of the 24 eyes of the 12 patients receiving transscleral cryotherapy, anatomical success was attained in 13 (81.3%) of 16 eyes.

Conclusions: This review found low GA and BBW to be major risk factors for ROP. This review shows that transscleral cryotherapy for treating threshold ROP achieved anatomical success in about 80% of eyes. However, myopia, amblyopia, and strabismus remain major sequelae. Laser therapy is now believed to be less damaging to ocular structures and just as effective as cryotherapy in treating ROP.

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Key words: retinopathy of prematurity, cryotherapy.

Retinopathy of prematurity (ROP), a retinal vascular disease and a frequent cause of blindness in infants, is nevertheless potentially preventable. Gestational age, birth body weight, and oxygenation are thought to be related to ROP. Ablation of the avascular peripheral retina with xenon arc photocoagulation was the first treatment,⁽¹⁾ then cryotherapy⁽²⁻⁵⁾ and more recently argon laser and diode laser photocoagulation have been used.⁽⁶⁻⁸⁾ Both cryotherapy and laser photocoagulation have been shown to

decrease the sequelae of ROP.^(4,9-12) The Cooperative Group showed that evaluation 5 years after treatment was associated with a 41% decrease in posterior retinal traction folds or detachments and a 19%~24% drop in the incidence of blindness.⁽²⁻⁴⁾ In this study, we reviewed data of infants who were evaluated for ROP over a 10-year interval for the main purpose of establishing possible risk factors, the incidence of ROP, and the effectiveness of cryotherapy for ROP in Taiwan.

From the Department of Ophthalmology, ¹Department of Pediatrics, Chang Gung Memorial Hospital, Keelung.

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Address for reprints: Dr. Tun-Lu Chen, Department of Ophthalmology, Chang Gung Memorial Hospital, 222, Maijin Rd., Anle Chiu, Keelung, Taiwan 204, R.O.C. Tel.: 886-2-24313131 ext. 2553; Fax: 886-2-24311190; E-mail: yangker@yam.com

METHODS

Institutional review board approval was obtained. This retrospective review surveyed data of all premature infants admitted to the neonatal intensive care unit who underwent ophthalmologic screening examinations for ROP between 1994 and 2003 in Keelung Chang Gung Memorial Hospital. Data were gathered from the eye examination log-book in the neonatal intensive care unit, ophthalmologist's records, and patients' medical charts. Gestational age (GA) was evaluated using prenatal estimates from data of the last menstrual period, prenatal sonograms (if available), and initial Ballard examinations. The first ophthalmologic screenings were executed by a vitreoretinal ophthalmologist (Ko-Jen Yang). Subsequent examinations were arranged every 2 to 3 weeks or sooner if advised by the ophthalmologist. Characteristics including gender, gestational age, birth body weight, initial stage of ROP, oxygen supplementation, blood transfusion, and treatment modalities, were collected and ana-

lyzed. ROP severity was gauged using The International Classification of Retinopathy of Prematurity.⁽¹³⁾ The initial stage of ROP was decided at the first consultation. Cryotherapy was performed for zone 2 threshold ROP in the presence of "plus" disease. Treatment was considered for confluent cryospots spaced 1 burn width apart. *t*-test and Chi-squared statistical analyses were performed, and all *p* values are 2-tailed test results.

RESULTS

Of the 458 infants who underwent ROP screening, there were 248 male and 210 female infants. Demographic characters are given in Table 1. Of the 148 eyes (Table 2) evaluated, in 74 premature infants showed evidence of ROP. Threshold ROP was detected in 24 eyes of 12 infants. The average birth body weight (BBW) and GA of infants with ROP were distinctly lower than those of the non-ROP group ($p < 0.05$, *t*-test). In comparing the use of oxygen and blood transfusions between the ROP and non-ROP group, no statistically significant difference appeared with the Chi-squared test. Of 12 patients who received cryotherapy, 3 expired and 1 was lost to follow-up. Macular dragging was found in 3 eyes, and anatomical success was achieved in 13 of 16 eyes (81.3%).

DISCUSSION

Current guidelines for initial ophthalmologic screening examinations in low-weight premature infants are based on the 1997 recommendations of the joint statement from the American Academy of

Table 1. Baseline Characteristics of Patients

Patients: 458 (916 eyes)	Male: 248 Female: 210
BBW (g)	1026.36 ± 498.39
GA (week)	31.20 ± 3.24
Initial screening time point (month)	5.54 ± 3.24
Initial stage of ROP (eye)	Non-ROP: 768
ROP: 148	Stage 1: 112 Stage 2: 32 Stage 3: 4

Abbreviations: BBW: birth body weight; GA: gestational age; ROP: retinopathy of prematurity.

Table 2. Characters of Infants with and without ROP

	ROP group (n = 148)	Non-ROP group (n = 768)	<i>p</i>
Mean BBW (g)	1301.63 ± 407.72	1813.97 ± 448.27	< 0.05
Mean GA (week)	29.13 ± 3.17	32.38 ± 2.19	< 0.05
Cryotherapy	13.5% (n = 20)	0.5% (n = 4)	
Blood transfusion (PRBC or FFP)	25.7%	23.2%	$\chi^2 < 3.84$ ($\alpha = 0.05$)
Supplemental oxygen	81.1%	80.6%	$\chi^2 < 3.84$ ($\alpha = 0.05$)

Abbreviations: SD: standard deviation; BBW: birth body weight; GA: gestational age; PRBC: packed red blood cells; FFP: fresh frozen plasma.

Pediatrics (AAP), the American Association for Pediatric Ophthalmology and Strabismus, and the American Academy of Ophthalmology.⁽¹⁴⁾ They suggest that in infants with a birth weight of ≤ 1500 g or with a gestational age (GA) of ≤ 28 weeks, screening should be done at a postmenstrual age (PMA) of 31 to 33 weeks, i.e., a chronological age of 4 to 6 weeks. This study found ROP in 36 eyes of infants whose BBWs were > 1500 g and GAs were > 28 weeks, whereas only 1 eye was diagnosed as being in ROP stage 2. All patients showed spontaneous regression, and none required further treatment. In addition, it seems that adequate medical support has lowered the ROP incidence in the most recent 5 years revealed in this study.⁽¹⁴⁾ Of the 12 infants requiring cryotherapy for threshold ROP with "plus" disease, 1 infant's gestational age was 29 weeks although his BBW was only 1024 g. These results confirm the validity of the current ROP screening guidelines.

In Cryo-Rop study, cryotherapy reduced unfavorable structural outcomes in threshold ROP from 47.9% in the untreated group to 27.2% in the treated group.⁽²⁾ Despite the advantages of cryotherapy, 44.4% of treated eyes had negative functional outcomes.^(3,4) Of the 12 patients with threshold ROP and "plus" disease in the present study, 3 expired and 1 was lost to follow-up. Of the remaining 8 patients, anatomical success was achieved in 13 eyes (81%), and this result compared favorably with the cryo-ROP study.⁽²⁻⁴⁾ Laser photocoagulation appears to produce structural and functional results at least as successful as those with cryotherapy.^(6,7,9,10,15-18) Shalev et al.⁽¹⁶⁾ compared ROP results following diode laser photocoagulation and cryotherapy in a 7-year study with 10 patients. They reported visual acuity and refractive error data which implied possible advantages for laser coagulation over cryotherapy. Possible adverse effects of cryotherapy include intraoperative bradycardia and apnea. Conjunctival lacerations, vitreous hemorrhage, and chemosis are frequently found postoperatively. However, because the laser spot is much smaller than the cryo-spot, as well as demanding precise laser aiming, laser photocoagulation is much more time-consuming. This in turn means that the depth and duration of anesthesia of these infants treated by laser photocoagulation are more critical than those treated by cryotherapy. There is a danger of over-sedation if infants become

agitated. Combined cryotherapy and diode laser photocoagulation are reported to be faster and technically simpler for ROP in very posterior locations.⁽¹⁹⁾

This review found no significant differences in the incidences of blood transfusion or oxygen supplementation between the ROP and non-ROP groups ($p > 0.05$). Blood transfusion volume and iron load by transfusion were reported to be linked to the risk of ROP in infants with a birth weight of less than 1250 g.⁽²⁰⁾ This link may exist because infants receiving more-frequent blood transfusions are also in a more-severe ischemic condition, which is itself believed to cause retinal vasoproliferation in ROP infants. While use of supplemental oxygen at pulse oximetry saturation levels of 96% to 99% have been reported not to cause additional progression of prethreshold ROP, it also did not noticeably lower the number of infants requiring ablative surgery.⁽²¹⁾ In addition the review demonstrated that clinicians need no longer worry that supplemental oxygen will worsen active prethreshold ROP. Because both cryotherapy and laser therapy are damaging, new treatments may supplant them in the future. New ways of preventing ROP may also evolve. For example, the effectiveness of vascular endothelial growth factor (VEGF) inhibitors in preventing retinal neovascularization is now being assessed.⁽²²⁾

As with the cryo-ROP study, this study found that low GA and BBW are major risk factors for ROP. Transscleral cryotherapy effectively prevents unfavorable results in threshold ROP. An approximately 80% anatomical success rate was shown in this review. Laser therapy is now believed to be less destructive to ocular structures and to be as effective as cryotherapy in ROP treatment. However, despite the advantages of treatment, intracranial problems, myopia, amblyopia, and strabismus remain major sequelae for these premature babies.⁽²³⁻²⁷⁾

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早產兒視網膜病變：基隆地區十年來之回顧

楊克仁 蔡振行 賴旗俊 呂嘉順 陳墩祿

背景：基隆地區10年來早產兒視網膜病變治療經驗之回顧。

方法：回顧統計基隆長庚醫院自1994至2003年間，所有早產兒照會的資料，收集分析包含性別、懷孕週數、出生體重，早產兒視網膜病變分期與治療結果。

結果：458位早產兒中，74位病人的148隻眼睛診斷有早產兒視網膜病變。12位病人的24隻眼睛診斷有臨界性早產兒視網膜病變加上正病變。發生早產兒視網膜病變的病人平均出生體重與懷孕週數都明顯低於無早產兒視網膜病變的病人 ($p < 0.05$)。而接受鞏膜外冷凍治療的24隻診斷有臨界性早產兒視網膜病變中，除了4位病人8隻眼睛因一些原因無法繼續追蹤，16隻眼睛內13隻眼睛術後成功抑制視網膜增殖性變化。

結論：本篇結果顯示出生體重與懷孕週數為早產兒視網膜病變的主要危險因子。鞏膜外冷凍治療有接近80%的成功率，但近視、弱視與斜視仍是主要的後遺症。雷射治療是目前認為對眼球構造較不具影響的治療方法。

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關鍵字：早產兒視網膜病變，視網膜冷凍治療。

長庚紀念醫院 基隆院區 眼科

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索取抽印本處：陳墩祿醫師，長庚紀念醫院 眼科。基隆市安樂區麥金路222號 Tel.: (02)24313131轉2553; Fax: (02)24311190; E-mail: yangker@yam.com