Treatment of type 1 retinopathy of prematurity with bevacizumab versus laser

Maram Isaac, MBBS, MHA,[a] Kamiar Mireskandari, MBChB, FRCSEd, FRCOphth, PhD,[a,b] and Nasrin Tehrani, MBBCh, MSc, FRCSEd Ophth, FRCSC[a,b]

PURPOSE To compare structural outcomes, visual function, refraction, and frequency of follow-up for infants with type 1 retinopathy of prematurity in zone I or zone II posterior treated with intravitreal bevacizumab (IVB) versus laser.

METHODS The medical records of infants treated with IVB or laser photocoagulation at our institution from January 2009 to May 2013 were retrospectively reviewed. Only infants with a minimum of 6 months' follow-up were included. Outcome measures were structural outcome, visual acuity, and spherical equivalent (SE) at corrected age of 1 year. The frequency of follow-up visits during 9 months after treatment was evaluated.

RESULTS A total of 23 eyes of 13 infants were treated with IVB and 22 eyes of 12 infants were treated with laser. There was no statistically significant difference in gestational age or birth weight between groups. None developed unfavorable structural outcome. Mean visual acuity was 0.99 ± 0.38 logMAR for the IVB group and 0.71 ± 0.36 logMAR for the laser group ($P = 0.34$; 95% CI, −0.52 to 0.19). Mean spherical equivalent was -3.57 ± 6.19 D for the IVB group and -6.39 ± 4.41 D for the laser group ($P = 0.33$; 95% CI, −7.19 to 2.49). In the IVB group, infants had an average of 16.00 ± 6.00 follow-up visits; in the laser group, 6.00 ± 3.00 ($P < 0.0001$).

CONCLUSIONS Both treatments resulted in good structural outcome, and no difference in visual acuity or refraction. However, more frequent follow-up was observed in the IVB group. (J AAPOS 2015;19:140-144)

Vascular endothelial growth factor (VEGF) is known to play a significant role in the pathogenesis of retinopathy of prematurity (ROP),[1] and intravitreal injection of anti-VEGF agents has become an accepted treatment for ROP. The most common agent used is off-label bevacizumab, which has proved efficacious for treatment of ROP.[2-6] The BEAT-ROP study (Bevacizumab Eliminates the Angiogenic Threat of Retinopathy of Prematurity) is the only randomized controlled trial that compared bevacizumab to laser for treatment of ROP.[4] It showed a higher failure rate with laser than bevacizumab. Recent studies have also reported a lower degree of myopia after bevacizumab treatment.[7-9] Bevacizumab treatment has also been shown to carry a risk for late recurrence and development of retinal detachment.[10,11] The current study aims to further elucidate structural outcomes, visual function, refraction, and frequency of follow-up visits for infants with type 1 ROP in zone I or zone II posterior[4] treated with intravitreal bevacizumab (IVB) versus laser for a follow-up period of 1 year of corrected age.

Methods

The medical records of all infants treated for type 1 ROP from January 2009 until May 2013 at the Hospital for Sick Children, Toronto, were retrospectively reviewed. Approval of the Research Ethics Board of the Hospital for Sick Children was obtained. Infants treated with intravitreal injection of bevacizumab or with retinal laser photocoagulation using diode laser 810 (Iris Medical Instruments Inc, Mountain View, CA) for type 1 ROP in zone I or zone II posterior were included. Bevacizumab was offered initially for select cases when the infant's general condition would not allow laser treatment. Following the publication of the BEAT-ROP study in 2011, treatment with bevacizumab was offered as a possible alternative to laser for treatment-requiring disease in zone I or zone II posterior.[4] Parents were provided with written information regarding the off-label use of bevacizumab, and the results of the Early Treatment for Retinopathy of Prematurity

Author affiliations: [a]Department of Ophthalmology and Vision Sciences, The Hospital for Sick Children, Toronto, Ontario, Canada; [b]Department of Ophthalmology and Vision Sciences, University of Toronto, Toronto, Ontario, Canada.

Brandan's Eye Research Foundation, Concord, Ontario, Canada, provided funding toward our department research fund.

Presented at the 40th Annual Meeting of the American Association for Pediatric Ophthalmology and Strabismus, Palm Springs, California, April 2-6, 2014, at the 2014 Annual Meeting of the Association for Research in Vision and Ophthalmology, Orlando, Florida, May 4-8, and at the 2014 Annual Meeting of the Canadian Ophthalmological Society, Halifax, Nova Scotia, June 4-7.

Submitted August 5, 2014.

Revision accepted January 8, 2015.

Correspondence: Nasrin Tehrani, MBBCh, MSc, FRCSEd Ophth, FRCSC, Department of Ophthalmology and Vision Sciences, The Hospital for Sick Children, 555 University Ave, Toronto, Ontario, Canada, M5G 1X8 (email: nasrin.tehrani@sickkids.ca).

1091-8531/$36.00

http://dx.doi.org/10.1016/j.jaapos.2015.01.009

Table 1. Baseline characteristics of infants treated with bevacizumab and laser

	Bevacizumab group	Laser group	*P* value, (95% CI for difference)
No. patients	13	12	
No. eyes	23	22	
BW, g, mean ± SD (median; range)	722 ± 131 (730; 540-920)	674 ± 175 (640; 433-1050)	0.44 (−175 to 78.92)
GA, weeks, mean ± SD (median; range)	25.2 ± 1.4 (25.1; 23.3-27.6)	25.0 ± 1.1 (24.8; 23.6-26.7)	0.69 (−1.27 to 0.85)
PMA at treatment, weeks, mean ± SD (median; range)	37.6 ± 1.7 (37.3; 35.3-41.7)	36.7 ± 2.6 (36.5; 33.1-41.6)	0.3 (−2.7 to 0.88)
Male/female	10/3	6/6	0.23 (0.56 to 20.0); OR = 3.33

BW, birth weight; *CI*, confidence interval; *GA*, gestational age; *OR*, odds ratio; *PMA*, postmenstrual age; *SD*, standard deviation.

(ETROP) and BEAT-ROP studies.[4,12] We explained to parents that the lack of long-term data on ocular or systemic safety and the paucity of data on long-term visual outcomes makes it impossible to know whether IVB treatment results in better visual acuity or field than laser treatment. Because of the risk of late disease reactivation, we also informed parents that infants receiving IVB require dilated fundus examinations with peripheral retinal examinations for a significantly longer period than laser-treated neonates. The parents were given time for careful consideration and were encouraged to discuss treatment options further with the treating ophthalmologist. The final decision to treat with laser or bevacizumab was made by parents.

Bevacizumab 0.625 mg/0.025 ml was injected into the vitreous cavity with a 30-gauge needle 1.0 mm posterior to the corneoscleral junction. All injections were performed in the neonatal intensive care unit under topical anesthesia.

The treating ophthalmologist's diagnosis of zone I ROP according to the International Classification of Retinopathy of Prematurity (ICROP) was accepted.[13] Two ophthalmologists reviewed fundus images (RetCam; Clarity Medical Systems, Pleasanton, CA) taken immediately before treatment to confirm the accuracy of zone diagnosis for each treated eye with zone II posterior allocation. Zone II posterior was defined as in the BEAT-ROP study as a circle with a radius originating at the optic disk and three times the distance between the center of the disk and the center of the macula.[4] Patients in whom the center of the macula could not be identified accurately on imaging were excluded.

Data on baseline characteristics, including sex, gestational age, birth weight, and postmenstrual age (PMA) at the time of treatment were collected. Primary outcome of the study was structural outcome at a corrected age of 1 year. Secondary outcome measures included visual acuity, refractive errors, and frequency of follow-up visits. Structural outcome was defined as in the ETROP.[12] Monocular grating visual acuity was collected for each treated eye, where available. Visual acuity was reported as in the ETROP study using conversion from cycles per degree into logMAR.[12] Visual acuity was divided into 4 categories; normal if it was ≤0.91 logMAR, subnormal if >0.91 and ≤1.2 logMAR, poor if it was >1.2 logMAR but measurable by standard acuity cards, and blind/low vision if no light perception. These categories were then grouped into favorable outcome that included eyes in the normal and subnormal categories, and unfavorable outcome that included eyes in the poor and blind categories. Refractive errors were recorded as spherical equivalent after cycloplegic refraction with cyclopentolate hydrochloride 1% at a corrected age of 1 year. Prevalence of myopia (≥0.25 D) and prevalence of high myopia (≥5.00 D) were calculated.[14-17]

Follow-up after laser treatment at our institution consists of seeing infants weekly until resolution of neovascularization and then as indicated by the patient's clinical need. IVB-treated infants are seen at 1 day after injection, then weekly until resolution of neovascularization, and thereafter according to response based on follow-up screening guidelines.[18] Follow-up beyond 45 weeks' PMA is individually tailored based on extent of retinal vascularization.

Frequency of follow-up visits during the first 9 months after treatment was assessed for each included infant. Nine months was chosen because reported cases of late recurrence and retinal detachment with IVB would have been expected to occur by this stage.[10,19]

Statistical analysis for continuous data was performed using two-sample *t* tests; the Fisher exact test was used for categorical data using SAS for Windows software version 9.3 (SAS Institute, Cary, NC). Repeated measures analysis (GEE model) was performed for visual acuity and spherical equivalent calculations. All *P* values were two sided and were considered statistically significant if <0.05.

Results

A total of 23 eyes of 13 infants were treated with IVB and 22 eyes of 12 infants were treated with laser. Table 1 shows baseline characteristics of the two groups. There was no statistically significant difference between groups. Table 2 shows indications for treatment in each group. All eyes were treated for type 1 ROP.

In the IVB group, all eyes received a single injection of 0.625 mg. Ten infants were treated in both eyes and 3 in one eye only. At last follow-up, no infant developed endophthalmitis, vitreous hemorrhage, cataract, or retinal detachment, and none of these eyes had developed a recurrence.

All 12 infants in the laser group were treated in both eyes. However, in 2 infants that had disease in zone II posterior, the other eye was treated for zone II posterior stage 3 preplus (type 2 ROP), and thus these two eyes were excluded from the analysis. Two weeks following treatment, one eye of an infant who had stage 3 with plus disease in zone I was found to have a small skipped area associated with persistent new vessels and was retreated with laser.

Table 2. Indication of treatment by zone, stage, and presence of plus disease in bevacizumab and laser treated groups

ROP parameter			Treatment group, no. eyes	
			Bevacizumab	Laser
Zone	Stage	Plus (Y/N)		
I				
	3	Y	5	6
	3	N	3	0
	2	Y	0	2
II posterior				
	3	Y	15	14

None of the eyes in our cohort developed unfavorable structural outcomes. In the IVB group, the regression of neovascularization was seen within 3-5 days after treatment and as early as within 24 hours. In the laser-treated group, there were 2 eyes that had increase in preexisting preretinal hemorrhage extending to the macular area after treatment. In these 2 eyes the hemorrhage resolved completely without structural sequelae.

Monocular visual acuity was measurable for 15 of 23 eyes (65%) in the IVB group at a mean corrected age of 11.06 ± 1.43 months (median 11; range 8.75-14.25) and for 18 of 22 eyes (82%) in the laser group at a mean corrected age of 12.1 ± 2.36 months (median, 12.75; range 7.75-15.0; *P* for difference in corrected age = 0.27; 95% CI, −0.87 to 2.96). The mean visual acuity for the IVB group was 0.99 ± 0.38 logMAR (median, 0.97; range, 0.5-1.68) and 0.71 ± 0.36 logMAR (median, 0.81; range, 0.0-1.1) for the laser group (*P* = 0.34; 95% CI, −0.52 to 0.19). Among eyes with measurable monocular visual acuity, favorable outcome was seen in 12 of 15 eyes (80%) in the IVB group and 18 of 18 eyes (100%) in the laser group (*P* = 0.08; 95% CI for difference, −0.4 to 0.002). The 3 eyes (20%) in the IVB group that had unfavorable visual outcome had visual acuity in the poor category.

Refraction was available for each treated eye. The mean spherical equivalent was −3.57 ± 6.19 D (median, −2.5 D; range, −15.0 to + 6.5 D) for the IVB group and −6.39 ± 4.41 D (median, −6.5 D; range, −13.0 to + 0.5 D) for the laser group (*P* = 0.33; 95% CI, −7.19 to 2.49), as shown in Figure 1. The mean corrected age at cycloplegic refraction was 10.81 ± 1.71 months (median, 11; range, 7.5-14.25) for the IVB group and 11.29 ± 2.58 months (median, 12.38; range, 7.25-14.25) for the laser group (*P* = 0.58; 95% CI, −1.31 to 2.28). The prevalence of myopia was 14 of 23 (61%) in the IVB group and 21 of 22 (95%) in the laser group (*P* = 0.076; OR, 0.124 [95% CI for difference, 0.012-1.23]). The prevalence of high myopia 8 of 23 (35%) in the IVB group and 13 of 22 (59%) in the laser group (*P* = 0.27, OR 0.44 [95% CI for difference, 0.10-1.92]).

The average number of eye examinations within the first 9 months after treatment for the IVB group was 16 ± 6 (median, 16; range 8-28), compared to 6 ± 3 examinations (median, 6; range, 4-14) in the laser group (*P* < 0.0001).

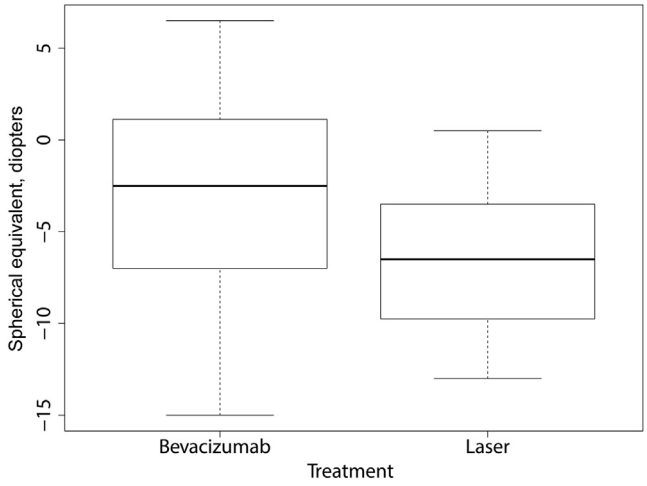

FIG 1. Box plot of the distribution of spherical equivalent refractive error in eyes of infants with type 1 retinopathy of prematurity in zone I or zone II posterior treated with intravitreal bevacizumab versus those treated with laser photocoagulation at one year of corrected age.

Discussion

Our study showed that treatment with either IVB or laser resulted in good response, with regression of neovascularization and favorable structural outcome. This is in keeping with the ETROP study, which reported 90.9% favorable structural outcome for type 1 ROP following laser ablation[12] and the BEAT-ROP study which showed that bevacizumab is more effective in the treatment of stage 3 with plus disease ROP than laser.[4] Significant treatment effect was shown for zone I but not zone II posterior.[4] Lack of recurrence in our patients is in contrast to the 6% recurrence in the BEAT-ROP study and lack of regression in 12% of eyes in a retrospective multicenter case series from Taiwan.[4,9] The difference in our study may be a reflection of the relatively small number of patients.

The present study found that IVB resulted in rapid regression of type 1 ROP in zone I and zone II posterior with a single injection of 0.625 mg bevacizumab, the same dose used in the BEAT-ROP study, which is half the adult dose.[4] Harder and colleagues[7] used a dose of 0.375 mg bevacizumab in 9 children with good response. Kuniyoshi and colleagues[20] used a dose of 0.25 mg bevacizumab in 8 eyes of 4 patients. This dose was found to be effective in 6 eyes with type 1 ROP in zone II posterior.[20] Additional treatment was required for the 2 eyes that had ROP in zone I. Spandau and colleagues[21] found progression of ROP in the 4 eyes they treated with higher dose bevacizumab 0.625 mg but not in 4 eyes treated with 0.4 mg. Further studies are needed to determine the lowest effective dose of bevacizumab that can enhance normal vascularization of retina with minimal systemic side effects.

Few studies have considered refractive errors following treatment with bevacizumab.[7-9,22,23] Table 3 summarizes

Table 3. Degree and prevalence of myopia in infants treated with intravitreal bevacizumab injection (IVB) in 4 studies

Study	Mean CA ± SD (range), months	No. eyes with refraction/total no. eyes	% eyes in zone I	Mean SE ± SD (range), D	Prevalence rate myopia, %	
					≥0.25 D	≥5.00 D
Current study	10.8 ± 1.71 (7.25-14.25)	23/23	35%	−3.57 ± 6.19 (−15 to +6.5)	61	35
Wu et al[9]	17.8 ± 7.6 (8.0-35.0)	53/162	10%	−0.1 ± 1.8 (−8.75 to 6.55)	NA	8
Harder et al[7]	11.1 ± 3.1 (7.0-23.0)	23/23	NA	−1.04 ± 4.24 (−12.5 to 4.63)	NA	17
Martinez-Castellanos et al[8]	12	9/9 (group 3 of reported patients)	NA	−1.09 ± 0.62 (−5.00 to 0.75)[a]	56[a]	11[a]
Geloneck et al[23]	30 ± 10.8[b]	110/140	47%	zone I: −1.5 ± 3.42 (−8.56 to 6.0); zone II posterior: −0.58 ± 2.53 (−13.0 to 2.5)	NA	11[c]
Chen et al[22]	24	40/40	NA	−0.98 ± 4.05	47.5	10

CA, corrected age; *D*, diopters; *NA*, not available; *SE*, spherical equivalent.
[a]Calculated from raw data provided in the original paper.
[b]For all infants enrolled in the study.
[c]For IVB treated eyes without recurrence as shown in Figure 4 in the original paper.

published results and those of the current study for mean spherical equivalent, prevalence of myopia, and high myopia. Previous studies reported a lower degree of myopia and high myopia compared to our IVB group. The ETROP results on the prevalence of myopia at 9 months reported that "the prevalence of myopia and high myopia tended to increase as the stage of ROP (severity) increased and with the presence of plus disease."[14] Also, in the early treatment group, eyes in zone I were more likely to have high myopia than those in zone II.[16] Inclusion of patients with more severe ROP may be one reason for the higher degree and prevalence of myopia observed in the current study.

Geloneck and colleagues[23] in the BEAT ROP study report on refractive outcomes at a mean age of 2.5 years showed a lower degree of myopia in both zone I (−1.51 ± 3.42 D) and zone II posterior (−0.58 ± 2.53 D) in the bevacizumab-treated group, which was significantly different from the laser treated group (−8.44 ± 7.57 D) for zone I and (−5.83 ± 5.87 D) for zone II posterior. All the eyes in their study had stage 3 plus disease and a large proportion of zone I disease in the IVB group. Therefore, in comparison to their study, severity of disease does not explain the higher rate and degree of myopia in our patients. The explanation may be in the difference in patient characteristics between their study and ours.

Our small sample size of 23 eyes is comparable to those of previously reported studies (Table 3). A larger sample size may be required to detect a statistically significant difference in rates of myopia between patients treated with IVB versus laser.

Our study showed no statistically significant difference in the mean visual acuity between IVB and laser groups at 12 months' corrected age. However, monocular visual acuity was measurable in only 65% for IVB eyes and in 82% of laser-treated eyes. Therefore our results should be interpreted with caution. The prospective study by Martinez-Castellanos and colleagues[8] found a higher rate of unfavorable visual acuity outcome at 12 months compared to our cohort (8/9 eyes in group 3). Of note, all 9 eyes in their study had progressed to favorable outcome at 3 years of follow-up.

To our knowledge, our study is the first to report on frequency of follow-up visits after IVB treatment. The difference in follow-up after IVB and laser (16 vs 6 visits) was statistically significant. Although we did not have any recurrence of ROP, not all retinas vascularized to the periphery. Lack of a definite end point as seen with laser is the main reason for longer and more frequent follow-up and the question remains whether avascular retina could potentially cause a recurrence requiring extended follow-up. The BEAT-ROP results showed that the mean time of recurrence was 16 weeks after treatment with IVB and recommended careful follow-up until completion of vascularization without active disease or clinically significant traction.[4] However, Moshfeghi and Berrocal[19] have argued that this follow-up period is inadequate to identify all potential recurrences and complications. At least 72.3 weeks' postmenstrual age was felt to be the required length of monitoring.[19] Indeed, Hu and colleagues[10] reported on a series of late retinal detachments following IVB treatments. The current lack of guidelines regarding frequency and length of follow-up after IVB may lead to significant stress on infants undergoing frequent follow-ups at an older age and can strain ophthalmological resources.[11]

Tahija and colleagues[24] used fluorescein angiography to evaluate extent of peripheral retinal vascularization following monotherapy with IVB for zone I and zone II posterior ROP. They observed that despite effectiveness of bevacizumab in achieving regression of neovascularization in posterior retina, 11 of 20 eyes did not have normal peripheral vascularization 6.75 to 56 months after treatment. Nine of 11 eyes had fluorescein leakage at the vascular avascular junction. Lepore and colleagues[25] in a randomized controlled trial showed extensive areas of peripheral avascular retina on fluorescein angiography performed 9 months after treatment with bevacizumab compared to the more typical retinochoroidal atrophy seen after laser treatment. Also, vascularization of the peripheral retina in normal infants may only be up to 2 disk

areas from the ora serrata.[26] All of the above factors complicate the safe end point of ROP screening in infants following IVB.

Although we did not encounter any unfavorable structural outcomes, a relatively short follow-up and small numbers limit our ability to comment on long-term effects or safety concerns and the ideal follow-up regimen.

In conclusion, in this cohort of infants, both bevacizumab and laser treatments resulted in good structural outcome. Furthermore, there was no statistically significant difference in the degree of myopia between groups. Failure of retinal vascularization for a prolonged period is a cause for concern and results in repetitive patient exposure to distressful eye examinations. A careful assessment of extent and rate of vascularization is important in managing this complicated retinal disease.

Literature Search

PubMed and MEDLINE (Ovid) were searched without date restriction for English-language results using a combination of medical subject headings (MeSH) and the following relevant keywords: *retinopathy of prematurity*, *treatment*, *bevacizumab*, *laser photocoagulation*, and *follow-up*.

Acknowledgments

The authors acknowledge Derek Stephens, biostatistician, clinical research services, the Hospital for Sick Children, Dalla Lana School of Public Health, University of Toronto, Toronto, Ontario, Canada, for his help in data analysis

References

1. Smith LE. Through the eyes of a child: understanding retinopathy through ROP the Friedenwald lecture. Invest Ophthalmol Vis Sci 2008;49:5177-82.
2. Chung EJ, Kim JH, Ahn HS, Koh HJ. Combination of laser photocoagulation and intravitreal bevacizumab (Avastin) for aggressive zone I retinopathy of prematurity. Graefes Arch Clin Exp Ophthalmol 2007; 245:1727-30.
3. Lalwani GA, Berrocal AM, Murray TG, et al. Off-label use of intravitreal bevacizumab (Avastin) for salvage treatment in progressive threshold retinopathy of prematurity. Retina 2008;28(3 Suppl): S13-18.
4. Mintz-Hittner HA, Kennedy KA, Chuang AZ. Efficacy of intravitreal bevacizumab for stage 3+ retinopathy of prematurity. N Engl J Med 2011;364:603-15.
5. Mintz-Hittner HA, Kuffel RR Jr. Intravitreal injection of bevacizumab (avastin) for treatment of stage 3 retinopathy of prematurity in zone I or posterior zone II. Retina 2008;28:831-8.
6. Travassos A, Teixeira S, Ferreira P, et al. Intravitreal bevacizumab in aggressive posterior retinopathy of prematurity. Ophthalmic Surg Lasers Imaging 2007;38:233-7.
7. Harder BC, Schlichtenbrede FC, von Baltz S, Jendritza W, Jendritza B, Jonas JB. Intravitreal bevacizumab for retinopathy of prematurity: refractive error results. Am J Ophthalmol 2013;155: 1119-1124.e1.
8. Martinez-Castellanos MA, Schwartz S, Hernandez-Rojas ML, et al. Long-term effect of antiangiogenic therapy for retinopathy of prematurity up to 5 years of follow-up. Retina 2013;33:329-38.
9. Wu WC, Kuo HK, Yeh PT, Yang CM, Lai CC, Chen SN. An updated study of the use of bevacizumab in the treatment of patients with prethreshold retinopathy of prematurity in Taiwan. Am J Ophthalmol 2013;155:150-158.e1.
10. Hu J, Blair MP, Shapiro MJ, Lichtenstein SJ, Galasso JM, Kapur R. Reactivation of retinopathy of prematurity after bevacizumab injection. Arch Ophthalmol 2012;130:1000-1006.
11. Mireskandari K, Adams GG, Tehrani NN. Recurrence of retinopathy of prematurity following bevacizumab monotherapy: is it only the tip of the iceberg? JAMA Ophthalmol 2013;131:544-5.
12. Early Treatment For Retinopathy Of Prematurity Cooperative Group. Revised indications for the treatment of retinopathy of prematurity: results of the early treatment for retinopathy of prematurity randomized trial. Arch Ophthalmol 2003;121:1684-94.
13. The International Classification of Retinopathy of Prematurity revisited. Arch Ophthalmol 2005;123:991-9.
14. Davitt BV, Dobson V, Good WV, et al; Early Treatment for Retinopathy of Prematurity Cooperative Group. Prevalence of myopia at 9 months in infants with high-risk prethreshold retinopathy of prematurity. Ophthalmology 2005;112:1564-8.
15. Quinn GE, Dobson V, Kivlin J, et al. Prevalence of myopia between 3 months and 5 1/2 years in preterm infants with and without retinopathy of prematurity. Ophthalmology 1998;105:1292-300.
16. Quinn GE, Dobson V, Davitt BV, et al; Early Treatment for Retinopathy of Prematurity Cooperative Group. Progression of myopia and high myopia in the Early Treatment for Retinopathy of Prematurity Study: findings to 3 years of age. Ophthalmology 2008;115: 1058-1064.e1.
17. Quinn GE, Dobson V, Davitt BV, et al; Early Treatment for Retinopathy of Prematurity Cooperative Group. Progression of myopia and high myopia in the Early Treatment for Retinopathy of Prematurity Study: findings at 4 to 6 years of age. J AAPOS 2013;17:124-8.
18. Jefferies Al. Retinopathy of prematurity: recommendations for screening. Paediatr Child Health 2010;15:667-70.
19. Moshfeghi DM, Berrocal AM. Retinopathy of prematurity in the time of bevacizumab: incorporating the BEAT-ROP results into clinical practice. Ophthalmology 2011;118:1227-8.
20. Kuniyoshi K, Sugioka K, Sakuramoto H, Kusaka S, Wada N, Shimomura Y. Intravitreal injection of bevacizumab for retinopathy of prematurity. Jpn J Ophthalmol 2014;58:237-43.
21. Spandau U, Tomic Z, Ewald U, Larsson E, Akerblom H, Holmström G. Time to consider a new treatment protocol for aggressive posterior retinopathy of prematurity? Acta Ophthalmol 2013;91:170-75.
22. Chen YH, Chen SN, Lien RI, et al. Refractive errors after the use of bevacizumab for the treatment of retinopathy of prematurity: 2-year outcomes. Eye (Lond) 2014;28:1080-86. quiz 1087.
23. Geloneck MM, Chuang AZ, Clark WL, et al; BEAT-ROP Cooperative Group. Refractive outcomes following bevacizumab monotherapy compared with conventional laser treatment: a randomized clinical trial. JAMA Ophthalmol 2014;132:1327-33.
24. Tahija SG, Hersetyati R, Lam GC, Kusaka S, McMenamin PG. Fluorescein angiographic observations of peripheral retinal vessel growth in infants after intravitreal injection of bevacizumab as sole therapy for zone I and posterior zone II retinopathy of prematurity. Br J Ophthalmol 2014;98:507-12.
25. Lepore D, Quinn GE, Molle F, et al. Intravitreal bevacizumab versus laser treatment in type 1 retinopathy of prematurity: report on fluorescein angiographic findings. Ophthalmology 2014;121:2212-19.
26. Blair MP, Shapiro MJ, Hartnett ME. Fluorescein angiography to estimate normal peripheral retinal nonperfusion in children. J AAPOS 2012;16:234-7.