Japanese Journal of Ophthalmology (2019) 63:262–268
https://doi.org/10.1007/s10384-019-00661-y

THE OFFICIAL INTERNATIONAL JOURNAL OF THE JAPANESE OPHTHALMOLOGICAL SOCIETY

CLINICAL INVESTIGATION

Short-term intraocular pressure changes after intravitreal injection of bevacizumab for retinopathy of prematurity

Atsuko Kato[1] · Yoshifumi Okamoto[1,2] · Fumiki Okamoto[1] · Makoto Saito[3] · Yayoi Miyazono[3] · Tetsuro Oshika[1]

Received: 29 July 2018 / Accepted: 21 December 2018 / Published online: 1 March 2019

Purpose To evaluate the short-term changes in intraocular pressure (IOP) after intravitreal injection of bevacizumab (IVB) in premature infants with retinopathy of prematurity (ROP).
Study design Prospective cohort study.
Methods Twenty-two eyes of 11 premature infants with ROP were evaluated. The control eyes were from adults who received an intravitreal injection of antivascular endothelial growth factor agent. The patients received a 0.025 mL (0.625 mg) IVB for the ROP. The IOP was measured with a rebound tonometer at baseline, immediately after the injection, and at 5, 10, 15, 20, and 30 minutes after the injection. The clinical data were collected. The main outcome measures were the IOP values at baseline, immediately after the injection, and at 5, 10, 15, 20, and 30 minutes after the injection.
Results The mean IOP values at baseline, immediately after the injection, and at 5, 10, 15, 20, and 30 minutes after the injection were 12.3 ± 3.0, 40.1 ± 10.7, 20.8 ± 5.1, 15.1 ± 4.8, 11.9 ± 3.2, 9.9 ± 2.6, and 8.8 ± 2.1 mmHg, respectively. The IOP was significantly higher at 5 minutes after the injection ($P < .01$); however, the pressure in all the eyes normalized (< 21 mmHg) within 15 minutes. None of the clinical parameters, including axial length, was correlated with a high IOP after IVB.
Conclusion In premature infants with ROP, IVB is tolerable in terms of the short-term elevation in IOP, which returned to a safe range (< 21 mmHg) within 15 minutes of the injection in all the patients. Consecutive IOP measurement might not be necessary after IVB in premature infants with ROP.

Keywords Intraocular pressure · Intravitreal injection of bevacizumab · Retinopathy of prematurity

Introduction

Retinopathy of prematurity (ROP) due to immaturity of retinal vascular proliferation is a potentially blinding condition and, with advances in perinatal care, has become a major cause of childhood blindness worldwide [1–4].

In recent years, intravitreal injection of bevacizumab (IVB) therapy has been reported as a useful option in addition to conventional laser treatment for preventing visual deterioration in premature infants with ROP [5–8]. However, contrary to the dramatic efficacy of IVB in premature infants with ROP, the complications associated with IVB for ROP have not been sufficiently evaluated. One of the complications of intravitreal injection of agents, including bevacizumab, is the acute elevation of intraocular pressure (IOP) [9–18]. Previous reports revealed that the elevated IOP potentially causes optic nerve damage such as glaucoma; moreover, a small number of adult patients may need eye-drop instillation following IVB treatment [10–12, 17, 18]. To the best of our knowledge, previously published studies have not assessed the short-term IOP transition after IVB in premature infants with ROP.

The purpose of this study was to evaluate the immediate and short-term IOP changes after IVB in premature infants

Corresponding Author: Yoshifumi Okamoto

✉ Yoshifumi Okamoto
y-okamoto@md.tsukuba.ac.jp

[1] Department of Ophthalmology, Faculty of Medicine, University of Tsukuba, 1-1-1 Tennodai, Tsukuba, Ibaraki 305-8575, Japan

[2] Department of Ophthalmology, Mito Kyodo General Hospital, Mito, Ibaraki, Japan

[3] Department of Pediatrics, Faculty of Medicine, University of Tsukuba, Tsukuba, Ibaraki, Japan

with ROP and to investigate the relationship between IOP elevation and the clinical parameters.

Patients and methods

This study was approved by the institutional review board of the University of Tsukuba Hospital and was conducted in adherence with the tenets of the Declaration of Helsinki. From September 2013 to March 2015, premature infants with a birth weight less than 1500 g or a gestational age younger than 35 weeks were screened for ROP in the neonatal intensive care unit of the University of Tsukuba Hospital by 2 ophthalmologists (Y.O., A.K.). The stage and severity of the ROP were classified in accordance with the International Classification of ROP (ICROP) [19, 20]. Threshold disease of ROP was defined in accordance with the criteria of the CRYO-ROP study [21]. Patients were excluded if they had a history of IVB (Avastin) or laser treatment for ROP, if they exhibited ocular disease that could affect the IOP and/or ocular morphology, or if they exhibited gastrointestinal dysfunction. Conventional laser treatment was performed in patients with systemic illnesses, such as gastrointestinal bleeding and cerebral hemorrhage, who were considered high-risk for IVB. The indication for IVB treatment was the development of threshold ROP in the aforementioned premature infants. The off-label use of IVB as an alternative to laser treatment was explained to the parents.

This prospective study included 22 eyes of 11 patients (7 male and 4 female) averaging 26.1 ± 2.7 gestational weeks (mean ± standard deviation) in age (range: 23–31 weeks). The demographic and clinical data were collected through chart review. We prepared the patients in a standard fashion, draped and positioned supine for the procedure. The patients' eyes were sterilized with a swab containing 10% povidone-iodine solution. Intravitreal bevacizumab (0.625 mg/0.025 cc) was performed through the temporal or nasal pars plana at 1.0 mm using a 30-gauge needle; the needle was aimed directly towards the optic nerve in the direction of the visual axis. The needle was inserted approximately 5 mm into the globe before the injection was performed. The IVB procedure was performed by 2 ophthalmologists (Y.O., A.K.). After the injection, a sterile cotton swab was placed on the injection site to prevent reflux of the medicine. All IVB therapy and IOP measurements were performed under general anesthesia by the neonatologist and using fentanyl citrate or midazolam. Intraocular pressure measurement was performed at baseline, immediately after the injection, and at 5, 10, 15, 20, and 30 minutes after the injection using a rebound tonometer (Icare PRO; Icare Finland Oy). The Icare PRO has been found to be a reliable method and has shown good correlation with Goldmann applanation tonometry [22]. The IOP measurements were ceased within 30 minutes of the IOP becoming lower than the preinjection IOP in consideration of the patient's systemic burden. Topical antibiotic drugs were administered for 3 days after the IVB. The refractive value at 1 year of age was measured with a handheld autorefractor (Retinomax K-plus; Nikon).

For comparison of the short-term IOP changes after IVB, intravitreal injections were performed in adult controls from February 2014 to October 2015. The controls comprised 4 patients with cystoid macular edema-induced branch retinal vein occlusion, 3 patients with age-related macular degeneration, and 2 patients with diabetic macular edema. All the controls were treatment-naïve and the exclusion criteria included patients with ophthalmic disorders other than original diseases or previous history of ocular surgery. After their informed consent was obtained, the patients received an intravitreal injection of antivascular endothelial growth factor (VEGF) agent (1.25 mg/0.05 cc) without paracentesis. The anti-VEGF agents used in the adult control group were ranibizumab in 5 eyes and aflibercept in 4 eyes. The axial length was measured manually using A-scan ultrasonography (AL-4000; Tomey).

The data were subjected to repeated-measures analysis of variance (ANOVA) to assess the time course of the changes. If significant differences were observed, the Dunnett test was performed. The data obtained from the eyes with ROP and the control eyes were also compared to evaluate any differences. The *t* test was used to detect differences between the 2 groups. Correlations between the highest IOP value after IVB and birth weight, gestational age, postmenstrual age at treatment, duration of hospitalization from birth to treatment, axial length at treatment, and refractive value at 1 year of age were analyzed using the Spearman rank correlation. Probability values below .05 were considered significant for all the comparisons. All statistical analyses were performed using StatView statistical software (version 5.0; SAS Institute).

Results

Table 1 summarizes the patients' clinical characteristics and parameters. The IVB procedure was successfully performed in all eyes; no serious intraprocedural or postprocedural complications (eg, cataract, intravitreal hemorrhage, retinal detachment, and endophthalmitis) were observed. Macroscopically, continuous reflux from the injection site was not observed in any of the premature infant cases. No participants, including the patients with ROP and the adult controls, had a systemic or critical disease after exposure to the antivascular endothelial growth factor (VEGF) agent during the study period. Additional IVB treatment was not needed in any of the patients with ROP; thus, IVB monotherapy in

Table 1 Clinical characteristics and ophthalmic parameters in patients undergoing intravitreal injection of bevacizumab for retinopathy of prematurity

Patient no.	Sex	Birth weight, g	Gestational age, wk	Postmenstrual age at treatment, wk	Duration of hospitalization from birth to treatment, d	Body weight at treatment, g	Axial length, mm (R/L)	Refractive value at 1 year of age (R/L)	Highest IOP after IVB, mmHg (R/L)
1	Female	1123	31.1	38.4	51	2209	18.11/18.99	1.5/0.875	24.8/24.2
2	Male	837	29.7	43.1	94	2340	18.33/18.34	-1.75/-2.125	40.4/41.4
3	Male	809	25.6	35.6	70	2204	-	-6.0/-4.125	64.8/48.3
4	Male	639	24.4	39	105	1693	19.68/18.65	-3.625/-4.0	34.9/42.0
5	Male	751	26.4	41.3	114	2780	16.80/16.76	-1.875/-1.625	32.3/40.3
6	Female	448	23.1	32.6	73	1003	-	0.625/-0.125	38.2/62.0
7	Male	517	23.1	34.1	78	1321	15.58/15.54	-5.5/-3.75	41.7/34.0
8	Male	499	28	37.2	65	1467	15.27/15.07	-	40.0/36.1
9	Male	740	26	38.5	90	2130	-	0.875/1.625	47.5/44.8
10	Female	672	24	40.3	115	1389	15.61/15.62	-	25.0/36.0
11	Female	982	29	29.1	75	2192	17.21/16.63	-3.25/-3.0	54.0/30.0
Average		729 ± 206	26.1 ± 2.7	38.2 ± 4.1	86 ± 21	1875 ± 541	17.01 ± 1.50	-1.96 ± 2.40	40.1 ± 10.7

Values are presented as means ± standard deviations

IOP intraocular pressure, *IVB* intravitreal injection of bevacizumab

this study could be used to successfully treat ROP until the retina was fully vascularized in the remaining eyes.

The baseline IOP before IVB in the premature infants with ROP was 12.3 ± 3.0 mmHg (range: 7.2–18.6). All the eyes had a baseline IOP of less than 20 mmHg. The average axial length in the premature infants with ROP was 17.01 ± 1.50 mm (range: 15.07–19.68), and 3 of the 11 patients (6 eyes) were excluded owing to inadequate accuracy. The highest mean IOP after IVB was 40.1 ± 10.7 mmHg (range: 24.2–64.8), which was recorded immediately after the IVB in all the cases. Of the 22 eyes with ROP, 12 eyes of 9 patients (54.5%) had an IOP greater than 40 mmHg, and 2 eyes of 2 patients (9.0%) had an IOP greater than 60 mmHg. No correlation was found between the highest IOP after IVB and any clinical parameters including birth weight ($P = .52$), gestational age ($P = .47$), postmenstrual age at treatment ($P = .32$), duration of hospitalization from birth to treatment ($P = .96$), body weight at treatment ($P = .86$), refractive value at 1 year of age ($P = .21$), and axial length at treatment ($P = .97$; Fig. 1).

Table 2 shows the time course of changes in IOP after the intravitreal injection of anti-VEGF agent in the patients with ROP and the adult controls. The eyes with ROP showed a sharp and transient elevation in IOP after the IVB; both immediately and 5 minutes after the IVB, the IOP was significantly higher than at baseline ($P < .05$, Dunnett test). No significant differences was found between the IOP at baseline and that after 10 minutes (ie, 10, 15, 20, and 30 minutes after the injection), and the IOP after 15 minutes (ie, 15, 20, and 30 minutes after the injection) tended to be lower than that at baseline ($P > .05$, Dunnett test). In the eyes with ROP, an IOP lower than the baseline measurement was observed in 10 of 21 eyes (47.6%) at 15 minutes, in 11 of 13 eyes (84.6%) at 20 minutes, and in 8 of 10 eyes (80.0%) at 30 minutes. The changes in IOP in the adult control group after intravitreal injection of anti-VEGF followed a similar trend to those of the ROP eyes, including a significantly higher IOP both immediately and at 5 minutes after the injection, compared with baseline ($P < .05$, Dunnett test).

When the IOP measurements of the eyes with ROP were compared with those of the control eyes, a significant difference in IOP was found between the 2 groups at all time points, including at baseline ($P < .05$). Table 2 shows the time course of IOP deviation from baseline after injection of anti-VEGF following adjustment of the baseline IOP between the 2 groups. The IOP of the premature infants with ROP was significantly lower than that of the control group at 15, 20, and 30 minutes ($P = .004$, .001, and .005, respectively). However, no significant difference in IOP was found between the 2 groups within the first 10 minutes (ie, immediately, 5, and 10 minutes after the injection), and the deviation in IOP in the premature infants with ROP tended to be lower than that in the adult controls throughout the study period.

Discussion

Since the BEAT-ROP study was published, the effectiveness of IVB in premature infants with ROP has been widely recognized [7]. However, the elevation in IOP associated

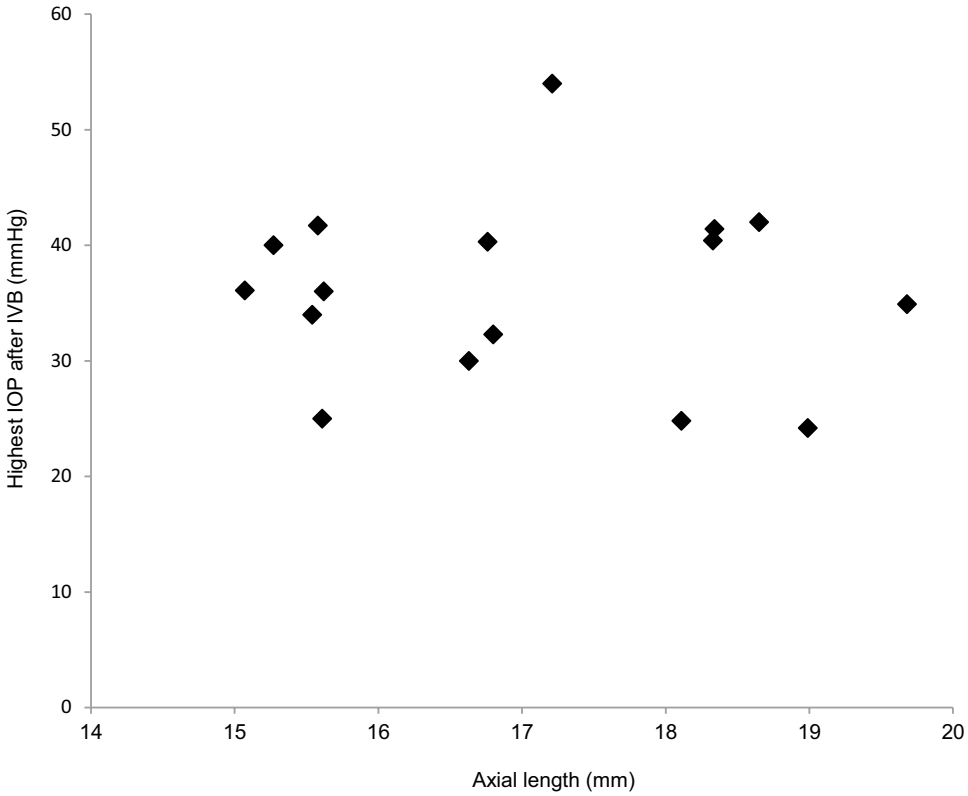

Fig. 1 Relationship between axial length and the highest intraocular pressure after intravitreal injection of bevacizumab for retinopathy of prematurity (16 eyes). *IOP* intraocular pressure, *IVB* intravitreal injection of bevacizumab

Table 2 Time course of changes in intraocular pressure after intravitreal injection of antivascular endothelial growth factor agents for retinopathy of prematurity and controls

	IOP, mmHg			Average deviation from baseline, mmHg		
	ROP (22 eyes)	Control (9 eyes)	*P* value	ROP	Control	*P* value
Baseline	12.3 ± 3.0	16.5 ± 2.2	< .001†	-	-	-
Immediately	40.1 ± 10.7*	50.2 ± 9.5*	.02†	27.9 ± 10.2	33.7 ± 9.2	.15
5 minutes	20.8 ± 5.1*	29.3 ± 9.3*	.002†	8.6 ± 4.6	12.8 ± 7.4	.06
10 minutes	15.1 ± 4.8	22.7 ± 6.4	.001†	2.9 ± 4.7	6.2 ± 4.6	.08
15 minutes	11.9 ± 3.2	21.2 ± 6.1	< .001†	-0.5 ± 4.1	4.7 ± 4.5	.004†
20 minutes	9.9 ± 2.6	20.3 ± 4.6	< .001†	-2.3 ± 2.2	3.2 ± 2.8	.001†
30 minutes	8.8 ± 2.1	17.7 ± 3.4	< .001†	-2.1 ± 2.6	1.2 ± 3.2	.005†

Values are presented as means ± standard deviations

ROP retinopathy of prematurity, *IOP* intraocular pressure

*Significant difference in intraocular pressure from baseline ($P < .05$, Dunnett test)

†Significant difference in intraocular pressure between the ROP eyes and the control eyes ($P < .05$, *t* test)

with IVB in premature infants with ROP was not clarified in the BEAT-ROP study. Therefore, the present study focused on the elevation of IOP as a complication following IVB in premature infants with ROP.

None of the patients with ROP in the present study required additional therapy after a single IVB, which was consistent with the positive results of the BEAT-ROP study (ie, the benefit of IVB monotherapy in premature infants with ROP was equivalent to or better than that of conventional laser). No ocular complications occurred during the BEAT-ROP study, but some complications have been reported in association with IVB in premature infants with ROP [23]. Although the positive effect of IVB treatment for ROP is becoming clearer, careful follow-up of these patients is needed to determine whether the effectiveness of IVB outweighs the risk of future complications.

In the present study, both the ROP patients and the adult controls, who received IVB and intravitreal injection of anti-VEGF agents, respectively, had a risk of short-term elevation in IOP. However, the elevation in IOP normalized rapidly

within 10 minutes in all the cases. These results suggest that consecutive IOP measurements are not necessary after IVB in premature infants with ROP. Patients with a history of glaucoma tend to have higher IOP after intravitreal injection than that of patients without glaucoma [10–12]. Because the long-term consequences of these transient events in premature infants with ROP are unknown, we should consider the possibility of sequelae.

The IOP in premature infants with ROP after IVB tended to be lower than the baseline IOP after 15 minutes and was significantly lower than that of the adult control group ($P < .05$). This might be because there was continuous reflux from the injection site after the needle was withdrawn. In the present study, we did not observe significant reflux from the injection site in any of the cases. However, it is possible that the fluid oozed very slowly from the injection site without a conjunctival bleb. Further investigation is necessary to determine whether the trend of lower IOP after IVB extends beyond 30 minutes.

In the present study, short-term IOP elevation was a demonstrated complication after each intravitreal injection. Many studies have reported that the rise in IOP peaked immediately after the intravitreal injection and decreased gradually within 30 minutes. In the present study, the majority (54.5%) of the patients who received IVB had an IOP greater than 40 mmHg, and 2 eyes (9.0%) had an IOP greater than 60 mmHg. Bui and colleagues [24] reported that an acute elevation in IOP of approximately 10 mmHg for 105 minutes has the potential to cause permanent dysfunction of the electroretinogram (ERG) in animal models and that there is a "threshold" for permanent retinal functional loss at an IOP of less than 60 mmHg. Because all of the cases in the present study recovered to the original IOP within 30 minutes, retinal damage is unlikely to have occurred. We did not investigate the systolic and diastolic blood pressures of the study candidates around the timing of the vitreous injection. Standard values of blood pressure in newborn infants differ according to the size and position of the cuff, as well as the physiological state of the infant; however, diastolic blood pressure in newborns is lower than the temporal rise of IOP, by as much as 60 mmHg [25]. Thus, it may induce retinal arterial occlusion. However, Hayreh and colleagues [26] reported that in old atherosclerotic hypertensive rhesus monkeys, no detectable damage occurred with 97 minutes of central retinal artery occlusion, whereas there was a variable degree of partial retinal recovery between 105 and 240 minutes, as indicated by the visual-evoked potential. Therefore, the elevation in IOP rapidly normalized within 10 minutes in all of the present cases; if retinal arterial occlusion occurred, retinal damage was undetectable.

To prevent increased IOP after intravitreal injection, preinjection paracentesis is an effective procedure in adult participants [27, 28]. However, the depth of the anterior chamber is smaller in a premature infant, and preinjection paracentesis has a greater potential to cause lens damage and subsequent amblyopia [29, 30]. Another possible method to prevent IOP elevation after intravitreal injection is to reduce the dose of the agents [31–33]. The elevation of IOP after intravitreal injection occurred in a dose-dependent manner. Low-dose IVB (0.25 mg/0.01 cc), or one-fifth of the standard dose, exhibited similar effectiveness for treatment of ROP to that of the standard dose IVB [32, 33]. These case series were limited by the small number of patients enrolled and uncertainty as to whether some premature infants might have been selected for laser treatment; nevertheless, they support the safety and effectiveness of a lower dose IVB for ROP.

In the present study, none of the parameters, including axial length, were correlated with a rise in IOP following IVB. In contrast, in the adult participants, the axial length was significantly correlated with IOP elevation after intravitreal injection [16, 18]. This difference may be explained by ocular biometry. Scleral thickness increases up to 2 years of age; thereafter, the thickness is independent of age and decreases with longer axial length [34]. Thus, axial length might not be correlated with elevation in IOP after IVB in premature infants with ROP.

Mild myopic changes were observed in the refractive value of patients at 1 year of age in the present study, which supports the results of previous studies [35–38]. Chen and colleagues [39] reported a higher refractive error after IVB than after intravitreal injection of ranibizumab in premature infants with ROP; this higher refractive error might have been caused by the longer half-life and longer suppression of VEGF. Chen and colleagues [39] thus suggested that lowering the dose of IVB might reduce the myopic shift commonly seen after IVB in premature infants with ROP. However, the cause of myopic progression after IVB in premature infants with ROP remains unknown. We hypothesize that acute and transient elevation in IOP might affect the ocular structure, causing changes in the refractive value; however, in this study, elevation in IOP was not associated with the refractive value. The amount of bevacizumab given to the premature infants (0.625 mg/0.025 cc) differed from that given to the adult controls (1.5 mg/0.05 cc). The vitreous has a volume of approximately 4 mL in the adult eye, or approximately 80% of the volume of the entire eye [40]. In the present study, the average axial length in the premature patients with ROP was 17.01 ± 1.50 mm; the volume of the entire eye is 2.06 mL in these patients. Thus, the vitreous volume is half that of the controls for premature infants with ROP. The difference in the volume of drug is not likely to cause a problem.

A limitation of the present study is that the presence of subconjunctival reflux was checked using a handheld slit lamp device. Significant bleb formation due to reflux was

not identified in any of the cases. However, wound configurations that are self-sealing in adults will often leak when used in children; moreover, children have thinner and less rigid sclera [41]. Thus, it is possible that the fluid oozed very slowly from the injection site. In the adult participants, reflux was noted in 48 of 152 eyes (31%), for which injection of anti-VEGF agents was given [42]. Further investigation is needed to evaluate the reflux rate after IVB in premature infants with ROP. Another potential study limitation is that measurement of the true highest IOP is impossible because of the delay before the start of IOP measurement after IVB. Conceivably, it might be possible that the true highest IOP is correlated with the clinical parameters in premature infants with ROP. The third potential study limitation is the accuracy of the IOP at higher levels (> 50 mmHg) with the iCare. Although the display range of the instrument is 0 to 99 mmHg, the measurement range is 7 to 50 mmHg. We found no papers in the literature regarding the accuracy of IOP at higher levels (> 50 mmHg) with the instrument. In the present study, 3 eyes of 3 patients had an IOP > 50 mmHg; it is possible that these values may lack accuracy. The fourth potential study limitation is that anesthetics may increase or decrease the IOP to a variable degree. All IOP measurements in the premature infants with ROP were performed under general anesthesia, using fentanyl citrate or midazolam. However, measurements in the adult controls were not performed under general anesthesia. Oberacher-Velten and colleagues [43] concluded that the feasibility of IOP measurements under sedation with midazolam, and the insignificant impact of orally administered midazolam on IOP, may be of benefit for glaucoma management in young children. Sator-Katzenschlager and colleagues [44] reported that general anesthesia with fentanyl as an analgesic reduces IOP in patients undergoing nonophthalmic surgery. General anesthesia using fentanyl citrate might decrease the IOP in premature patients with ROP.

In conclusion, IVB in premature infants with ROP was tolerable with respect to the short-term elevation in IOP, as all the patients' IOP returned to a safe range (< 21 mmHg) within 15 minutes. The systemic status of the patient at birth or at treatment, the axial length, and the refractive value at 1 year of age were not correlated with elevation in IOP after IVB. Therefore, consecutive measurements of IOP might not be necessary after IVB in premature infants with ROP.

Conflicts of interest A. Kato, None; Y. Okamoto, None; F. Okamoto, None; M. Saito, None; Y. Miyazono, None; T. Oshika, None.

References

1. Stefansson E. How to prevent retinopathy of prematurity. Acta Ophthalmol. 2011;89:3–4.
2. Shah PK, Prabhu V, Karandikar SS, Ranjan R, Narendran V, Kalpana N. Retinopathy of prematurity: past, present and future. World J Clin Pediatr. 2016;8:35–46.
3. Murakami Y, Silva RA, Jain A, Lad EM, Gandhi J, Moshfeghi DM. Stanford University Network for Diagnosis of Retinopathy of Prematurity (SUNDROP): 24-month experience with telemedicine screening. Acta Opthalmol. 2010;88:317–22.
4. Quinn GE. Retinopathy of prematurity blindnesss worldwide: phenotypes in the third epidemic. Eye Brain. 2016;8:31–6.
5. Wang J, Xiang D. Early clinical characteristics of bacterial endophthalmitis in retinopathy of prematurity after intravitreal bevacizumab injection: a case report. Exp Ther Med. 2017;13:3563–6.
6. Mintz-Hittner HA. The use of anti-VEGF intravitreal injections for vision threatening stage 3 retinopathy of prematurity: risk-benefit ratio. Retina. 2009;29:562–4.
7. Mintz-Hittner HA, Kennedy KA, Chuang AZ; BEAT-ROP Cooperative Group. Efficacy of intravitreal bevacizumab for stage 3+ retinopathy of prematurity. N Engl J Med. 2011;364:603–15.
8. 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.
9. Benz MS, Albini TA, Holz ER, Lakhanpal RR, Westfall AC, Iyer MN, et al. Short-term course of intraocular pressure after intravitreal injection of triamcinolone acetonide. Ophthalmology. 2006;113:1174–8.
10. Frenkel RE, Mani L, Toler AR, Frenkel MP. Intraocular pressure effects of pegaptanib (Macugen) injections in patients with and without glaucoma. Am J Ophthalmol. 2007;143:1034–5.
11. Bakri SJ, Pulido JS, McCannel CA, Hodge DO, Diehl N, Hillemeier J. Immediate intraocular pressure changes following intravitreal injections of triamcinolone, pegaptanib, and bevacizumab. Eye (Lond). 2009;23:181–5.
12. Kim JE, Mantravadi AV, Hur EY, Covert DJ. Short-term intraocular pressure changes immediately after intravitreal injections of anti-vascular endothelial growth factor agents. Am J Ophthalmol. 2008;146:930–4.
13. Hollands H, Wong J, Bruen R, Campbell RJ, Sharma S, Gale J. Short-term intraocular pressure changes after intravitreal injection of bevacizumab. Can J Ophthalmol. 2007;42:807–11.
14. Singh IP, Ahmad SI, Yeh D, Challa P, Herndon LW, Allingham RR, et al. Early rapid rise in intraocular pressure after intravitreal triamcinolone acetonide injection. Am J Ophthalmol. 2004;138:286–7.
15. Bakri SJ, Beer PM. The effect of intravitreal triamcinolone acetonide on intraocular pressure. Ophthalmic Surg Lasers Imaging. 2003;34:386–90.
16. Cacciamani A, Oddone F, Parravano M, Scarinci F, Di Nicola M, Lofoco G. Intravitreal injection of bevacizumab: changes in intraocular pressure related to ocular axial length. Jpn J Ophthalmol. 2013;57:63–7.
17. Murray CD, Wood D, Allgar V, Walters G, Gale RP. Short-term intraocular pressure trends following intravitreal ranibizumab injections for neovascular age-related macular degeneration: the role of oral acetazolamide in protecting glaucoma patients. Eye (Lond). 2014;28:1218–22.
18. Song S, Yu XB, Dai H. Effect of prophylactic intraocular pressure-lowering medication (brinzolamide) on intraocular pressure after ranibizumab intravitreal injection: a case-control study. Indian J Ophthalmol. 2016;64:762–6.
19. An international classification of retinopathy of prematurity. The committee for the classification of retinopathy of prematurity. Arch Ophthalmol. 1984;102:1130–4.
20. ICROP Committee for Classification of Late Stages ROP. An international classification of retinopathy of prematurity, II:

the classification of retinal detachment. Arch Ophthalmol. 1987;105:906–12.
21. Cryotherapy for retinopathy of prematurity cooperative group. Multicenter trial of cryotherapy for retinopathy of prematurity. Arch Ophthalmol. 1988;106:471–9.
22. Kim KN, Jeoung JW, Park KH, Yang MK, Kim DM. Comparison of the new rebound tonometer with Goldman applanation tonometer in a clinical setting. Acta Ophthalmol. 2013;91:e392–6.
23. Chhablani J, Rani PK, Balakrishnan D, Jalali S. Unusual adverse choroidal reaction to intravitreal bevacizumab in aggressive posterior retinopathy of prematurity: the Indian Twin Cities ROP screening (ITCROPS) data base report number 7. Semin Ophthalmol. 2014;29:222–5.
24. Bui BV, Batcha AH, Fletcher E, Wong VH, Fortune B. Relationship between the magnitude of intraocular pressure during an episode of acute elevation and retinal damage four weeks later in rats. PLoS One. 2013;29:e70513.
25. Pejovic B, Peco-Antic A, Marinkovic-Eric J. Blood pressure in non-critically ill preterm and full-term neonates. Pediatri Nephrol. 2007;22:249–57.
26. Hayreh SS, Zimmerman MB, Kimura A, Sanon A. Central retinal artery occlusion: retinal survival time. Exp Eye Res. 2004;78:723–36.
27. Lorenz K, Zwiener I, Mirshahi A. Subconjunctival reflux and need for paracentesis after intravitreal injection of 0.1 ml bevacizumab: comparison between 27-gauge and 30-gauge needle. Graefes Arch Clin Exp Ophthalmol. 2010;248:1573–7.
28. Soheilian M, Karimi S, Montahae T, Nikkhah H, Mosavi SA. Effects of intravitreal injection of bevacizumab with or without anterior chamber paracentesis on intraocular pressure and peripapillary retinal nerve fiber layer thickness: a prospective study. Graefes Arch Clin Exp Ophthalmol. 2017;255:1705–12.
29. O'Brien C, Clark D. Ocular biometry in pre-term infants without retinopathy of prematurity. Eye (Lond). 1994;8:662–5.
30. Kent D, Pennie F, Laws D, White S, Clark D. The influence of retinopathy of prematurity on ocular growth. Eye (Lond). 2000;14:23–9.
31. Harder BC, von Baltz S, Jonas BJ, Schlichtenbrede FC. Intravitreal low-dosage bevacizumab for retinopathy of prematurity. Acta Ophthalmol. 2014;92:577–81.
32. Khodabande A, Niyousha MR, Roohipoor R. A lower dose of intravitreal bevacizumab effectively treats retinopathy of prematurity. J AAPOS. 2016;20:490–2.
33. Connor AJ, Papastavrou VT, Hillier RJ, Shafiq A. Ultra-low-dose intravitreal bevacizumab for the treatment of prematurity. J Pediatr Ophthalmol Strabismus. 2015;52:20–1.
34. Shen L, You QS, Xu X, Gao F, Li B, Jonas JB. Scleral thickness in Chinese eyes. Invest Ophthalmol Vis Sci. 2015;56:2720–7.
35. Chen YH, Chen SN, Lien RI, Shih CP, Chao AN, Chen KJ, et al. Refractive errors after the use of bevacizumab for the treatment of retinopathy of prematurity: 2-year outcomes. Eye (Lond). 2014;28:1080–6.
36. Hwang CK, Hubbard GB, Hutchinson AK, Lambert SR. Outcomes after intravitreal bevacizumab versus laser photocoagulation for retinopathy of prematurity: a 5-year retrospective analysis. Ophthalmology. 2015;122:1008–15.
37. Geloneck MM, Chuang AZ, Clark WL, Hunt MG, Norman AA, Packwood EA, et al. Refractive outcomes following bevacizumab monotherapy compared with conventional laser treatment. JAMA Ophthalmol. 2014;132:1327–33.
38. Gunay M, Sekeroglu MA, Bardak H, Celik G, Esenulku CM, Hekimoglu E, et al. Evaluation of refractive errors and ocular biometric outcomes after intravitreal bevacizumab for retinopathy of prematurity. Strabismus. 2016;24:84–8.
39. Chen SN, Lian I, Hwang YC, Chen YH, Chang YC, Lee KH, et al. Intravitreal anti-vascular endothelial growth factor treatment for retinopathy of prematurity: comparison between ranibizumab and bevacizumab. Retina. 2015;35:667–74.
40. Brod RD. Surgery for diseases of the vitreous and retina. J Lancaster Gen Hosp. 2009;4:4–9.
41. Basti S, Krishnamachary M, Gupta S. Results of sutures wound construction in children undergoing cataract extraction. J Pediatr Ophthalmol Strabimus. 1996;33:52–4.
42. Usman Saeed M, Batra R, Qureshi F, Clark D. Reflux of drug during intra-vitreal anti-VEGF therapies. Semin Ophthalmol. 2011;26:357–60.
43. Oberacher-Velten I, Prasser C, Rochon J, Ittner KP, Helbig H, Lorenz B. The effects of midazolam on intraocular pressure in children during examination under sedation. Br J Ophthalmol. 2011;95:1102–5.
44. Sator-Katzenschlager SM, Oehmke MJ, Deusch E, Dolezal S, Heinze G, Wedrich A. Effects of remifentanil and fentanyl on intraocular pressure during the maintenance and recovery of anaesthesia in patients undergoing non-ophthalmic surgery. Eur J Anaesthesiol. 2004;21:95–100.