Review Article

# Refractive outcomes in infants treated for retinopathy of prematurity

Fatemeh Heidary [1] and Reza Gharebaghi [1]

[1] *International Virtual Ophthalmic Research Center, Austin, Texas, United States*

**ABSTRACT**

**Background:** Infants treated for retinopathy of prematurity (ROP) can develop visually significant refractive error. However, the degree of refractive error may differ between laser treatment and intravitreal anti-vascular endothelial growth factor (anti-VEGF) injection. We reviewed studies that investigated refractive error outcomes of treatment in premature infants with ROP.

**Methods:** In this narrative review, a literature search was carried out in PubMed/MEDLINE from 01/01/2000 to 20/10/2022 without language restrictions, using the following keywords: "anti-VEGF," "ROP" or "prematurity retinopathy," and "laser." We included comparative studies on refractive error outcomes of intravitreal anti-VEGF and laser treatments, a combination of both modalities simultaneously or sequentially, and two anti-VEGF agents.

**Results:** The initial search yielded 164 records. We reviewed the titles and abstracts of the retrieved papers and the reference list of published systematic reviews and meta-analyses, meta-analyses, or reviews on our topic. Thirty-three records fulfilled our inclusion criteria, which included refractive outcomes in 4350 eyes of 2359 participants treated for ROP. Based on the reported refractive outcomes, we divided the studies into four categories: 1) those that revealed a higher rate of refractive error in the laser-treated eyes than in the anti-VEGF-treated eyes; 2) those that revealed no significant difference in refractive outcomes between the two treatment modalities; 3) those that revealed a higher rate of refractive error in the anti-VEGF-treated eyes or compared refractive outcomes between two anti-VEGF agents; and 4) those that reported refractive outcomes in the eyes that received combined simultaneous or sequential treatment with laser after initial anti-VEGF treatment. We also summarized the refractive outcomes of all included primary studies in each category.

**Conclusions:** This study showed that the laser-treated eyes experienced more myopic shift. However, the refractive outcomes in premature infants of laser treatment, anti-VEGF treatment, and a combination of both modalities simultaneously or sequentially were often contradictory. This variability resulted from obvious differences in the sample size, different follow-up durations, or inhomogeneous study or treatment designs. Further well-designed prospective trials on refractive outcomes and the trend of changes in the refractive status over long-term follow-ups in the eyes treated with ROP are necessary to identify consensus results concerning real-world refractive outcomes of each treatment modality or simultaneous or sequential combination of both modalities, to suggest a safe and effective treatment option for eye care professionals.

**KEYWORDS**

infant, neonate, premature infant, retinopathy of prematurity, refractive error, laser therapy, intravitreal injection, vascular endothelial growth factor, anti-VEGF

**Correspondence:** Reza Gharabaghi, International Virtual Ophthalmic Research Center, Suite No 4000, 5900 Balcones Drive, STE 100, Austin, Texas, 78731, United States, Tel: +1 (281) 8990369. Email: drgharebaghi@yahoo.com. ORCID iD: https://orcid.org/0000-0002-4906-8597

**How to cite this article:** Heidary F, Gharebaghi R. Refractive outcomes in infants treated for retinopathy of prematurity. Med Hypothesis Discov Innov Optom. 2022 Fall; 3(3): 96-105. https://doi.org/10.51329/mehdioptometry157

Received: 30 October 2022; Accepted: 23 December 2022

## INTRODUCTION

Aberrations in refractive development are serious sequelae of retinopathy of prematurity (ROP) [1]. The eyes treated with ROP are likely to develop myopia during early childhood. Likewise, the prevalence of the eyes with high myopia was increased between the ages of 6 months and 3 years [2]. Laser and intravitreal injection of anti-vascular endothelial growth factor (anti-VEGF) treatments are current treatment modalities for ROP [2-4].

During laser monotherapy, numerous children with a history of ROP develop myopia and high astigmatism. The myopia is lenticular, and a longer axial length causes the development of high myopia. Furthermore, refraction at 1 year can predict the future development of myopia [5]. Most diode laser-treated eyes with a threshold ROP develop myopia. Anisometropia, which is a significant risk factor for poor visual outcomes, is also noted in approximately one-half of the patients [6].

A review of articles on anti-VEGF monotherapy for ROP in 466 eyes revealed a prevalence of high myopia of 0% – 35%. Anti-VEGF monotherapy caused less myopia and decreased the incidence of high myopia [7]. Similarly, another systematic review and meta-analysis of randomized or quasi-randomized controlled trials revealed a reduced risk of refractive errors during childhood after anti-VEGF monotherapy [4]. Although outcomes have been promising, anti-VEGF treatment for ROP is still a new approach, and the long-term safety and determination of the optimum dose are yet to be determined [7].

Anti-VEGF monotherapy in the eyes treated for severe ROP leads to a lower prevalence of myopia compared to laser treatment. Similarly, lower anisometropia develops after anti-VEGF monotherapy, with similar levels of significant astigmatism between the two treatment modalities [1]. In school children with a history of laser-treated type 1 ROP, the eyes developed a significantly higher degree of myopia compared to those with a history of anti-VEGF monotherapy. The latter group also had favorable developmental outcomes despite similar vision [8]. In contrast, another study on the treatment-requiring ROP eyes revealed no significant difference in the myopia status between laser and anti-VEGF treatment at 3 years of age [9].

However, combined systematic reviews and meta-analyses, meta-analyses, or reviews [3, 4, 10-15] comparing the laser-treated eyes with anti-VEGF monotherapy revealed that anti-VEGF injection caused less myopia, a lower prevalence of high myopia or astigmatism, and an overall lower risk of refractive errors in childhood. A subgroup analysis revealed a higher degree of myopia in aggressive posterior ROP than in type 1 ROP [11].

Not all studies have reported reduced myopia with anti-VEGF than with laser treatment [9, 16], and there are no consensus results concerning the refractive outcomes of each treatment modality. In this narrative review, we summarized recent evidence on refractive outcomes in premature infants with ROP between anti-VEGF and laser-treated treatments, a combination of both modalities simultaneously or sequentially, and two anti-VEGF agents.

## METHODS

A literature search was carried out in PubMed/MEDLINE from 01/01/2020 to 20/10/2022 without language restrictions, using various combinations of the following keywords: "anti-VEGF," "ROP" or "prematurity retinopathy," and "laser." We included primary studies comparing refractive outcomes in the eyes with ROP between laser treatment and anti-VEGF agents, different anti-VEGF agents, and a combination of both modalities simultaneously or sequentially.

## RESULTS

We reviewed the titles and abstracts of 164 records and reference lists of published systematic reviews and meta-analyses, meta-analyses, and reviews. Thirty-three records fulfilled the inclusion criteria. Overall, the refractive outcomes of 2359 participants and 4350 eyes treated for ROP had been analyzed and reported.

Major risk factors of ROP are early gestational age (GA) and low birth weight (BW) [17, 18]. In a study by Etezad Razavi et al. [19] involving 38 premature infants' eyes treated with intravitreal bevacizumab (IVB) monotherapy (76 eyes), GA and spherical equivalent of refractive error (SEQ) showed no significant correlation, but BW and SEQ at a 1-year adjusted age showed a significant correlation. In the eyes with spontaneously regressed ROP (98 eyes of 49 infants), GA and SEQ or BW and SEQ showed no significant correlation. At 1 year of age, refractive outcomes showed no significant difference between the IVB-treated eyes and the eyes with spontaneous regression of ROP [19]. Thus, parameters other than BW and GA, such as the treatment modality, may also play a role in the development of refractive errors in the eyes treated for ROP.

Based on the reported refractive outcomes, we divided the studies into four categories: 1) those that revealed a lower rate of refractive error in the anti-VEGF treated eyes [20-22]; 2) those that revealed no significant difference in refractive outcomes between the two treatment modalities [9, 16, 23]; 3) those that revealed a higher rate of refractive error in the anti-VEGF treated eyes [24] or compared refractive outcomes between two anti-VEGF agents [25-27]; and 4) those that reported refractive outcome of sequential treatment with laser after initial anti-VEGF treatment [28, 29]. Table 1 summarizes the refractive outcomes reported in the 33 primary studies.

Of the 33 papers, 14, including 2475 eyes of 1281 premature infants treated for ROP, reported a lesser degree of myopia with anti-VEGF treatment than with laser treatment (Table 1). However, nine papers, including 1046 eyes of 547 premature infants treated for ROP, reported similar refractive outcomes between the two treatment modalities (Table 1). In a study by Vujanovic et al. [30], refractive astigmatism and high myopia were more common in the laser-treated eyes, and anisometropia was significantly greater than that in the anti-VEGF-treated eyes. Therefore, this study was included in the first category. However, as the frequency of myopia did not differ significantly between the two treatment modalities, these results were also mentioned in the results of the studies in the second category (Table 1).

The third category consisted of seven papers, including 481 eyes of 337 premature infants, comparing refraction outcomes of anti-VEGF and laser treatments [24], bevacizumab and ranibizumab [25-27, 31], or reported refraction outcomes of bevacizumab monotherapy [32, 33] (Table 1). Despite low levels of myopia in the anti-VEGF-treated eyes, refractive outcomes differed with the anti-VEGF agent, with the eyes treated with bevacizumab being significantly more myopic [25, 26]. However, bevacizumab led to a lower rate of ROP recurrence than ranibizumab [15].

The fourth category consisted of four papers, including 480 eyes of 260 premature infants, reporting refractive outcomes of sequential [28, 29, 34] or combined laser and anti-VEGF treatments [35] (Table 1).

**Table 1. Summary of refractive outcomes in 4350 anti-VEGF or laser-treated eyes of 2359 premature infants with ROP**

| Author (Year of Publication) | Numbers of included infants / eyes | An evidence-based summary of refractive outcomes |
|---|---|---|
| **Studies included in the first category** | | |
| **Gundlach et al. (2022) [20]** | 175 infants / 350 eyes | Primary anti-VEGF treatment had a significantly lower incidence of amblyopia but no significant difference in the rate of myopia compared to primary laser treatment. Laser treatment was associated with the development of severe myopia and amblyopia. |
| **Simmons et al. (2021) [1]** | 48 children / 48 eyes | Despite similar refractive errors at the initial visit, the laser-treated eyes had a significantly more myopic shift compared to the anti-VEGF-treated eyes during the first 3.5 years of age. The prevalence of significant anisometropia was comparable between the two treatment modalities. At the final visit, the mean (SD, range) SEQ in the laser- and anti-VEGF-treated eyes were - 8.00 D (5.84 D, - 20.00 to + 3.50 D) and - 2.38 D (4.18 D, - 10.00 to + 2.75 D), respectively. During the first 1.1 years, the anti-VEGF-treated eyes showed a significant decrease in SEQ over time at an average rate of - 3.5 D/year, but the laser-treated eyes showed a significantly faster rate of SEQ change (- 5.0 D/year). However, after 1.1 years, this rate became significantly slower for both treatment modalities. |
| **Chen et al. (2020) [8]** | 25 children / 47 eyes | In school-aged children with a history of type 1 ROP, the laser-treated eyes had a significantly higher degree of myopia compared to the anti-VEGF-treated eyes. |
| **Kang et al. (2019) [36]** | 165 children / 314 eyes | Refractive error at the most recent follow-up (mean [SD] follow-up duration of 36.3 [31.9] months) had a significantly stronger association with myopia in the laser-treated eyes with type 1 ROP (SEQ: - 1.09 D) compared to the anti-VEGF-treated eyes (SEQ: + 0.11 D). |
| **Lee et al. (2018) [37]** | 42 children / 80 eyes | The anti-VEGF-treated eyes had lesser myopia, better uncorrected visual acuity, and comparable best-corrected visual acuity compared to the laser-treated eyes or eyes treated with a combination of both modalities. |
| **Roohipoor et al. (2018) [38]** | 493 infants / 986 eyes | The mean (SD) spherical power and SEQ were significantly higher in the laser-treated eyes than in the anti-VEGF treated eyes, with no significant differences in the astigmatic power. |
| **Vujanovic et al. (2017) [30]*** | 66 children / 132 eyes | At the 9-month follow-up examining cycloplegic refraction, high hypermetropia was significantly more common in the laser-treated eyes (15.6%) than in the anti-VEGF-treated eyes (11.9%). Astigmatism was more common in the laser-treated eyes (81.1%) than in the anti-VEGF-treated eyes (71.4%), particularly with high astigmatism. Anisometropia was significantly greater in the laser-treated eyes (24.4%) than in the anti-VEGF-treated eyes (9.5%). High myopia (SEQ < - 3.0 D) was more common in the laser-treated eyes (18.9%) than in the anti-VEGF-treated eyes (16.7%). |

**Continued Table 1. Summary of refractive outcomes in 4350 anti-VEGF or laser-treated eyes of 2359 premature infants with ROP**

| | | |
|---|---|---|
| **O'Keeffe et al (2016)** [39] | 15 children / 30 eyes | At the 5-year follow-up, less myopia was detected in the anti-VEGF-treated eyes compared to the laser-treated eyes. |
| **Gunay et al. (2015)** [40] | 40 children / 78 eyes | At the 2-year follow-up, the anti-VEGF-treated eyes with aggressive posterior ROP (0.42 [3.42] D) were significantly less myopic compared to the laser-treated eyes (- 6.66 [4.96] D). Rates of anisometropia and strabismus were significantly higher in the laser-treated eyes compared to the anti-VEGF treated eyes. |
| **Hwang et al. (2014)** [41] | 28 children / 54 eyes | The mean SEQs at the last refraction for the anti-VEGF- and laser-treated eyes were - 2.4 and - 5.3 D, respectively. The mean SEQs for the zone I and II ROP eyes treated with anti-VEGF treatment were - 3.7 and 0.6 D, respectively, and for those treated with laser treatment were - 10.1 and - 4.7 D, respectively. The eyes with type 1 ROP treated with anti-VEGF treatment (at 22.4 months) had less myopia compared to the laser-treated eyes (at 37.1 months), but the laser-treated eyes had a longer follow-up. |
| **Geloneck et al. (2014)** [21] | 109 infants / 211 eyes | The mean (SD) SEQ was significantly lower in the anti-VEGF-treated eyes with ROP in zone I (- 1.51 [3.42] D) than in the laser-treated eyes (- 8.44 [7.57] D) and in the anti-VEGF-treated eyes with ROP in posterior zone II (- 0.58 [2.53] D) than in the laser-treated eyes (- 5.83 [5.87] D). Very high myopia (≥ - 8.00 D) was significantly more common in the laser-treated eyes with ROP in zone I (51.4%) than in the anti-VEGF-treated eyes (3.8%) and in the laser-treated eyes with ROP in posterior zone II (36.4%) than in the anti-VEGF treated eyes (1.7%). |
| **Chen et al. (2014)** [42] | 34 children / 64 eyes | At the age of 2 years, 47.5% and 10.0% of the anti-VEGF-treated eyes with severe ROP had myopia and high myopia, respectively, which were significantly less than those treated with a combination of anti-VEGF and laser treatments (82.4 and 29.4%, respectively), and the anti-VEGF-treated eyes were more likely to remain emmetrope. |
| **Harder et al. (2013)** [22] | 25 children / 49 eyes | At the end of the follow-up, the anti-VEGF-treated eyes were significantly less myopic than the laser-treated eyes (- 1.04 [4.24] and - 4.41 [5.50] D, respectively). The prevalence of moderate and high myopia was significantly lower in the anti-VEGF-treated eyes, which had a significantly lower refractive astigmatism. In the multivariate analysis, myopia and astigmatism were significantly associated with laser treatment. At the 1-year follow-up, the anti-VEGF-treated eyes had less myopia and astigmatism compared to the laser-treated eyes. |
| **Harder et al. (2012)** [43] | 16 children / 32 eyes | The refractive status of the anti-VEGF-treated eyes with threshold ROP in posterior zone II or I or prethreshold ROP in zone I at 10.5 (2.7) months of corrected age was compared to that of the laser-treated eyes at 11.5 (1.0) months of corrected age. The mean refractive errors of both eyes were significantly less myopic in the anti-VEGF-treated group, but refractive astigmatism was comparable between groups. |
| **Studies included in the second category** | | |
| **Kang et al. (2019)** [44] | 27 children / 52 eyes | Refraction at 4 years of age revealed no significant difference in mean SEQ between the anti-VEGF- and laser-treated eyes with ROP. |
| **Roohipoor et al. (2018)** [45] | 116 infants / 232 eyes | Infants with type 1 ROP in zone II (stage 2 or 3 ROP with plus disease) were randomly allocated to the anti-VEGF or laser treatment group and showed comparable spherical and cylindrical refractive errors at a postmenstrual age of 90 weeks. |
| **Kabatas et al. (2017)** [46] | 54 children / 108 eyes | At 18 months, mean (SD) SEQ was - 1.49 (3.04) D in intravitreal bevacizumab monotherapy, - 1.79 (2.87) D in intravitreal ranibizumab monotherapy, and - 1.27 (2.80) D in laser treatment, which were comparable. The magnitude of astigmatism did not differ significantly among groups. |
| **Vujanovic et al. (2017)** [30]* | 66 children / 132 eyes | At the 9-month follow-up examining cycloplegic refraction, the frequency of myopia or clinically significant hypermetropia or axial length did not differ significantly between the anti-VEGF- and laser-treated eyes. |
| **Gunay et al. (2017)** [47] | 134 children / 264 eyes | At an adjusted age of 1.5 years, the mean SEQ did not differ significantly between the laser-treated eyes and eyes treated with either anti-VEGF agent. However, the laser-treated eyes with ROP in zone I had a significantly higher rate of myopia and high myopia than those treated with either anti-VEGF agent. |
| **Mueller et al. (2017)** [23] | 54 children / 108 eyes | At the 12-month follow-up, SEQ was comparable between the anti-VEGF- and laser-treated eyes with posterior ROP. However, the anti-VEGF-treated eyes with posterior ROP had a significantly lower SEQ (+ 0.37 D) compared to the anti-VEGF-treated eyes with peripheral zone II ROP (+ 3.0 D). |
| **Gunay et al. (2016)** [48] | 42 children / 76 eyes | Infants with ROP at an adjusted 1-year age showed no significant differences in the myopic status between anti-VEGF and laser treatment groups. |

**Continued Table 1. Summary of refractive outcomes in 4350 anti-VEGF or laser-treated eyes of 2359 premature infants with ROP**

| | | |
|---|---|---|
| **Kuo et al. (2015)** [9] | 29 children / 29 eyes | Cycloplegic refraction at 3 years of age revealed no significant difference in the myopic status between the anti-VEGF- and laser-treated eyes. |
| **Isaac et al. (2015)** [16] | 25 children / 45 eyes | The mean visual acuity and SEQ at a corrected age of 1 year were comparable between the anti-VEGF- and laser-treated eyes. The mean (SD) visual acuity for the anti-VEGF treated eyes was 0.99 (0.38) logMAR and for the laser-treated eyes was 0.71 (0.36) logMAR. The mean (SD) SEQ was - 3.57 (6.19) D for the anti-VEGF-treated eyes and - 6.39 (4.41) D for the laser-treated eyes. The average number of follow-up visits was significantly higher for the anti-VEGF-treated eyes. |
| **Studies included in the third category** | | |
| **Adams et al. (2018)** [24] | 168 children / 168 eyes | Refractive outcomes at the 1-year follow-up of the treated eyes with ROP revealed that the proportion of the eyes with myopia ≥ - 5 D was the highest in infants with type 1 ROP (31% after anti-VEGF treatment and 5.3% after laser treatment) and that the overall proportion of the eyes with myopia ≥ - 5 D was higher in the anti-VEGF- (26.3%) than in laser-treated infants (6.7%). |
| **Kimyon et al. (2018)** [25] | 37 children / 68 eyes | At an adjusted 1-year age in post-anti-VEGF treatment for the eyes with type 1 ROP in zone I, the mean (SD) SEQs in the bevacizumab- and ranibizumab-treated eyes were - 1.49 (2.38) and 0.98 (2.18) D, respectively, with significantly more myopia in the bevacizumab-treated eyes. |
| **Chen et al. (2018)** [26] | 33 children / 62 eyes | Comparing refractive statuses of the eyes with type 1 ROP post-anti-VEGF treatment at a corrected age of 3 years revealed that the frequency of the eyes with a refractive error > 1 D and high myopia (< - 5.0 D) was significantly higher in the bevacizumab group than in the ranibizumab group. |
| **Lin et al. (2016)** [27] | 21 children / 40 eyes | At the 1-year post-anti-VEGF treatment follow-up of the eyes with a threshold ROP, the mean (SD) SEQs in the bevacizumab- and ranibizumab-treated eyes were comparable at - 0.60 (3.86) and 0.46 (1.36) D, respectively. |
| **Chen et al. (2015)** [31] | 37 children / 72 eyes | The anti-VEGF-treated eyes (bevacizumab or ranibizumab) with type 1 ROP had minor mean refractive errors at a corrected age of 1 year. |
| **Wu et al. (2013)** [32] | 28 children / 53 eyes | At 18 months of age, infants with the anti-VEGF-treated eyes had a mean (SD, range) spherical power, cylindrical power, and SEQ of 0.8 (2.6, - 6.3 to 7.3 D), - 2.1 (1.1 D, - 5.3 to - 0.3 D), and - 0.1 (1.8 D, - 8.75 to 6.55 D), respectively, with 8% having SEQ > - 5.0 D [32]. These findings were parallel with the refractive data of the eyes with subthreshold ROP without treatment, which showed a mean (range) SEQ refractive error of - 0.22 (- 9 to + 2.25 D) at 36 months and were significantly less myopic than the cryotherapy- or laser-treated eyes [49]. |
| **Martinez-Castellanos et al. (2013)** [33] | 13 infants / 18 eyes | The anti-VEGF-treated eyes with ROP were followed-up over the 5-year period. Eleven (61%) had myopia (≥ - 0.5 D) at 12 months, which increased to 12 eyes at 60 months with a mean myopic change of < 1 D in 4 years. Two-thirds of the eyes had low myopia (≤ - 3 D) at 60 months, and eyes with high-risk prethreshold or threshold ROP had the most favorable outcome (mean myopia of - 1.75 D). |
| **Studies included in the fourth category** | | |
| **Hoppe et al. (2022)** [28] | 34 infants / 68 eyes | Infants with type 1 ROP treated with the anti-VEGF and delayed laser treatments, at least 2 weeks and < 1 year after the initial anti-VEGF injection [28], developed lower rates of high myopia compared to those with a history of laser monotherapy [2]. |
| **Bayramoglu et al. (2022)** [29] | 181 infants / 331 eyes | After primary anti-VEGF treatment in infants with ROP, the extents of pre-treatment and pre-laser retinal vascularization were associated with the development of ≥ - 1 D myopia at a mean (SD) age of 22.9 (10.9) months, without additional laser treatment. |
| **Gangwe et al. (2021)** [34] | 32 infants / 63 eyes | Infants with aggressive posterior ROP after primary anti-VEGF treatment were randomly allocated to a delayed (laser at 6 weeks or earlier in case of recurrence of plus disease) or an early (laser at 1 week) laser treatment group. The eyes in the former group required fewer laser spots. At 6 months, the eyes in the former group were less myopic than those in the latter. |
| **Araz-Ersan et al. (2015)** [35] | 13 children / 18 eyes | Children with a history of combined anti-VEGF and laser treatments for type 1 ROP had comparable spherical or cylindrical refractive errors as the laser-treated eyes at 2 years of age. |

**Abbreviations: ROP, retinopathy of prematurity; VEGF, vascular endothelial growth factor; SD, standard deviation; SEQ, spherical equivalent of refractive error; D, diopters; logMAR, logarithm of the minimum angle of resolution. Note:*considering the results, we presented this study in two categories.**

## DISCUSSION

Most studies concluded that the laser-treated eyes experienced more myopic shift [1, 8, 20-22, 30, 36-43]. Overall, anti-VEGF monotherapy resulted in low myopia. In a comparative interventional case series, Lee et al. found that anti-VEGF monotherapy led to less myopia and better uncorrected visual acuity compared to laser treatment or a combination of anti-VEGF and laser treatments [37].

Geloneck et al. [21] in a randomized controlled trial allocated the eyes in the anti-VEGF and laser treatment groups, with a mean (standard deviation [SD]) age of 2.5 (0.9) years at the time of refraction, who had a comparable GA and BW. The mean (SD) SEQs in the eyes with zone I ROP and without recurrence in the anti-VEGF and laser treatment groups were - 1.36 (3.34) and - 7.34 (7.44) D, respectively, while in the eyes with zone II posterior ROP and without recurrence in the anti-VEGF and laser treatment groups were - 0.63 (2.56) and - 5.20 (5.77) D, respectively. The SEQ was significantly lower in the anti-VEGF-treated eyes than in the laser-treated eyes [21].

Harder et al. [22] investigated refractive outcomes in a retrospective study involving 23 eyes treated with the anti-VEGF monotherapy and 26 eyes treated with laser treatment with comparable GA and BW over a 1-year follow-up. At a mean (SD) follow-up of 11.4 (2.3) months after birth, the anti-VEGF-treated eyes were significantly less myopic compared to the laser-treated eyes (mean [SD]: - 1.04 [4.24] versus - 4.41 [5.50] D), with less moderate myopia (17% versus 54%), less high myopia (9% versus 42%), and lower refractive astigmatism (mean [SD]: - 1.0 [1.04] versus 1.82 [1.41] D). They concluded that a single administration of anti-VEGF caused less myopization and astigmatism compared to laser treatment [22].

Gunay et al. [40] investigated refractive outcomes in a retrospective study involving 48 eyes in the anti-VEGF treatment group and 30 eyes in the laser treatment group during a mean period of 2 years with comparable mean GA (26.40 and 27.30 weeks, respectively), BW (901.40 and 941.00 g, respectively), and sex distribution. The mean (SD) SEQ was 0.42 (3.42) D (range: - 8.75 to + 5.00 D) in the anti-VEGF-treated eyes and - 6.66 (4.96) D (range: - 15.5 to + 1.75 D) in the laser-treated eyes. The anti-VEGF monotherapy-treated eyes were significantly less myopic compared to the laser-treated eyes at 2 years. The laser-treated eyes had significantly higher rates of anisometropia and strabismus compared to the anti-VEGF-treated eyes [40].

Roohipoor et al. [38] conducted a retrospective case series study involving 724 (73.4%) eyes in the anti-VEGF and 262 (26.5%) eyes in the laser treatment group and found that the mean (SD) of the sphere and SEQ were significantly higher in the laser-treated eyes (- 1.31 [2.83] and -2.84 [2.77] D, respectively) than in the anti-VEGF-treated eyes (0.19 [3.21] and - 1.26 [3.19] D, respectively), but the cylindrical power was comparable. The last refraction was performed at the mean (SD) post-GA of 27.2 (7.7) months (range: 19 to 35 months) in the anti-VEGF group and 24.1 (14.8) months (range: 9 to 39 months) in the laser treatment group [38].

Some studies revealed comparable refractive outcomes between the two treatment modalities for ROP [9, 16, 23, 30, 44-48]. The treatment type did not influence long-term refractive outcomes in ROP [44]. Isaac et al. [16] included 23 eyes in the anti-VEGF treatment group and 22 eyes in the laser treatment group and compared SEQ at a corrected age of 1 year and found no significant difference in the visual acuity or SEQ. The mean (SD) SEQ in the anti-VEGF- and laser-treated eyes were -3.57 (6.19) and - 6.39 (4.41) D, respectively [16].

Kuo et al. [9] investigated refractive outcomes in a retrospective comparative study involving 14 eyes in the laser treatment group and 15 eyes in the anti-VEGF treatment group at 3 years of age, with comparable GA (27.43 [2.93] versus 27.33 [2.94] weeks) and BW (1006.79 [327.65] versus 1079.67 [357.48] g). The mean (SD) SEQs at 3 years of age in the laser- and VEGF-treated eyes were - 1.71 (1.27) D (range: - 4.375 to 0.125 D) and - 1.53 (2.20) D (range: - 5.875 to 1.500 D), respectively. The eyes with type 1 ROP in the laser and anti-VEGF treatment groups had similar refraction and myopic status [9].

In a retrospective comparative study, Mueller et al. [23] followed-up the anti-VEGF and laser-treated eyes up to 12 – 15 months of age. The SEQ at 12 months after treatment was comparable between the two treatment groups in patients with posterior ROP and peripheral zone II. The SEQ was significantly lower in the laser-treated eyes with posterior zone II ROP than in the IVB-treated eyes with peripheral zone II ROP, without significant difference in visual acuity. Furthermore, the anti-VEGF-treated eyes with posterior ROP had a significantly lower SEQ (+ 0.37 D) compared to the anti-VEGF-treated eyes with peripheral zone II ROP (+ 3.0 D) [23].

The third category of papers reported a higher proportion of myopia between the anti-VEGF- and laser-treated eyes [24] and bevacizumab- and ranibizumab-treated eyes [25, 26]. Chen et al. [31] found comparable mean refractive errors for the two anti-VEGFs with a significantly higher chance of high myopia in the bevacizumab treated eyes. In addition, a minor myopic shift was reported in the eyes treated with bevacizumab alone [32, 33] (Table 1).

Despite low levels of myopia in the anti-VEGF-treated eyes, refractive outcomes may differ with specifically administered anti-VEGF agents, with the bevacizumab-treated eyes being significantly more myopic [25, 26, 31]. However, Lin et al. [27] found comparable refractive outcomes for the two anti-VEGFs. Though, bevacizumab can lead to a lower ROP recurrence rate compared to ranibizumab [15].

Adams et al. [24] conducted a longitudinal national surveillance study involving 168 children and reported refractive outcomes for the eyes treated for ROP. Refractive outcomes at the 1-year follow-up of the treated eyes with ROP revealed that the proportion of eyes with myopia ≥ - 5 D was the highest in infants with type 1 ROP (31% after anti-VEGF treatment and 5.3% after laser treatment) and that the overall proportion of the eyes with myopia ≥ - 5 D was greater in the anti-VEGF group (26.3%) than in the laser-treated infants (6.7%) [24].

Four studies were included in the fourth category concerning refractive outcomes [28, 29, 34, 35]. Recently published studies on potential therapeutic benefits of the anti-VEGF and laser combination treatment have shown promising outcomes [29, 34, 35]. Laser treatment may still be required as an additional treatment for patients not responding to the IVB injection or for those in whom ROP worsens after the IVB injection [32]. Laser treatment may be more efficacious in managing ROP with a significantly lower retreatment incidence than anti-VEGF treatment, and supplemental laser ablative treatment could reduce recurrence after initial anti-VEGF treatment [12, 15]. However, myopia decreased significantly more with anti-VEGF treatment than with laser treatment [12, 14].

Infants with type 1 ROP treated with anti-VEGF and delayed laser treatments, at least 2 weeks and < 1 year after the initial anti-VEGF injection, developed lower rates of high myopia [28] compared to those with a history of laser monotherapy [28, 2]. After primary anti-VEGF treatment in infants with ROP, the extents of pre-treatment and pre-laser retinal vascularization were associated with the development of ≥ 1 D myopia at a mean (SD) age of 22.9 (10.9) months, without additional laser treatment [29]. Large-scale randomized trials with a longer follow-up to evaluate anti-VEGF monotherapy in comparison with anti-VEGF and laser combination treatment are necessary to assess whether or not adverse effects of laser and general anesthesia outweigh their benefits in terms of preventing ROP reactivation associated with anti-VEGF monotherapy [28, 50, 51].

This review summarized the recent evidence on refractive outcomes in the eyes treated for ROP. Results of the primary studies showed variability stemming from differences in the sample size, follow-up duration, or inhomogeneous study or treatment designs. However, our interpretation should be verified using systematic reviews or meta-analyses. Considering the inclusive nature of systematic reviews, we may have overlooked some available primary studies. Our review failed to follow a systematic review or meta-analysis protocol, which could have provided more practical outcomes. However, because systematic reviews are narrow in scope, we decided to take advantage of conventional reviews to provide a broad overview of this topic. The current literature on this topic has no consensus results and indicates the necessity for future well-designed prospective trials. Finally, since a higher degree of myopia in aggressive posterior ROP than in type 1 ROP [11] was reported in the subgroup analysis, future studies should elucidate whether the observed refractive status in the treated eyes is a function of the treatment modality or protocol or depends on the zone of involvement (The anti-VEGF-treated eyes with posterior ROP developed a significantly lower SEQ compared to the anti-VEGF-treated eyes with peripheral zone II [23]) or stage of ROP (With random allocation of the eyes with stage 2 or 3 ROP to the anti-VEGF or laser treatment group, comparable spherical and cylindrical refractive outcomes were found at a postmenstrual age of 90 weeks [45]), or both. Moreover, the impact of child age factor should be investigated over a long follow-up, as after 1.1 years, the rate of SEQ change was significantly slower for both treatment modalities [1].

## CONCLUSIONS

In addition to age-related deterioration of the eye in complicated ROP, a major reason for vision loss is anisometropia and refractive errors. The treatment modality could predict the refractive outcomes during the follow-up. Almost half of the included studies reported that the laser-treated eyes experienced a more myopic shift. However, the refractive outcomes in treating ROP of premature infants compared between post-laser and anti-VEGF treatments, post-anti-VEGF agents, and a combination of both modalities simultaneously or sequentially were often contradictory. This variability resulted from differences in the sample sizes, follow-up durations, or inhomogeneous study or treatment designs of the included studies. Further well-designed prospective trials on refractive outcomes and the trend of changes in the refractive status over long follow-ups in the eyes treated with ROP are necessary to identify consensus results concerning real-world refractive outcomes of each treatment modality or simultaneous or sequential combination of both modalities. Timely correction of refractive errors and anisometropia are critical in this group of children. This finding might be useful for ophthalmologists and optometrists in prescribing glasses and preventing amblyopia in patients with ROP.

## ETHICAL DECLARATIONS

**Ethical approval:** No ethical approval was required.
**Conflict of interests:** Dr. Fatemeh Heidary was assigned as the Editor in Chief of Medical hypothesis, discovery & innovation in optometry.


## FUNDING

**None.**

## ACKNOWLEDGMENTS

Articles submitted by the board, staff, and Editor-in-Chief of this journal are also subjected to peer review. These types of papers have been handled by another person on the editorial board (without conflicts of interest), and in all processes, those who had a conflict of interest were not involved.


## REFERENCES


1. Simmons M, Wang J, Leffler JN, Li S, Morale SE, de la Cruz A, et al. Longitudinal Development of Refractive Error in Children Treated With Intravitreal Bevacizumab or Laser for Retinopathy of Prematurity. Transl Vis Sci Technol. 2021;10(4):14. doi: 10.1167/tvst.10.4.14 pmid: 34003992
2. Quinn GE, Dobson V, Davitt BV, Wallace DK, Hardy RJ, Tung B, 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(2):124-8. doi: 10.1016/j.jaapos.2012.10.025 pmid: 23622444
3. Tan QQ, Christiansen SP, Wang J. Development of refractive error in children treated for retinopathy of prematurity with anti-vascular endothelial growth factor (anti-VEGF) agents: A meta-analysis and systematic review. PLoS One. 2019;14(12):e0225643. doi: 10.1371/journal.pone.0225643 pmid: 31790445
4. Sankar MJ, Sankar J, Mehta M, Bhat V, Srinivasan R. Anti-vascular endothelial growth factor (VEGF) drugs for treatment of retinopathy of prematurity. Cochrane Database Syst Rev. 2016;2:CD009734. doi: 10.1002/14651858.CD009734.pub2. Update in: Cochrane Database Syst Rev. 2018;1:CD009734 pmid: 26932750
5. Kaur S, Sukhija J, Katoch D, Sharma M, Samanta R, Dogra MR. Refractive and ocular biometric profile of children with a history of laser treatment for retinopathy of prematurity. Indian J Ophthalmol. 2017;65(9):835-840. doi: 10.4103/ijo.IJO_872_16 pmid: 28905827
6. Yang CS, Wang AG, Sung CS, Hsu WM, Lee FL, Lee SM. Long-term visual outcomes of laser-treated threshold retinopathy of prematurity: a study of refractive status at 7 years. Eye (Lond). 2010;24(1):14-20. doi: 10.1038/eye.2009.63 pmid: 19343053
7. Mintz-Hittner HA, Geloneck MM. Review of effects of anti-VEGF treatment on refractive error. Eye Brain. 2016;8:135-140. doi: 10.2147/EB.S99306 pmid: 28539808
8. Chen YC, Chen SN. Foveal microvasculature, refractive errors, optical biometry and their correlations in school-aged children with retinopathy of prematurity after intravitreal antivascular endothelial growth factors or laser photocoagulation. Br J Ophthalmol. 2020;104(5):691-696. doi: 10.1136/bjophthalmol-2019-314610 pmid: 31420328
9. Kuo HK, Sun IT, Chung MY, Chen YH. Refractive Error in Patients with Retinopathy of Prematurity after Laser Photocoagulation or Bevacizumab Monotherapy. Ophthalmologica. 2015;234(4):211-7. doi: 10.1159/000439182 pmid: 26393895
10. Kong Q, Ming WK, Mi XS. Refractive outcomes after intravitreal injection of antivascular endothelial growth factor versus laser photocoagulation for retinopathy of prematurity: a meta-analysis. BMJ Open. 2021;11(2):e042384. doi: 10.1136/bmjopen-2020-042384 pmid: 33568373
11. Wang SD, Zhang GM; Shenzhen Screening for Retinopathy of Prematurity Cooperative Group. Laser therapy versus intravitreal injection of anti-VEGF agents in monotherapy of ROP: a Meta-analysis. Int J Ophthalmol. 2020;13(5):806-815. doi: 10.18240/ijo.2020.05.17 pmid: 32420230
12. Li Z, Zhang Y, Liao Y, Zeng R, Zeng P, Lan Y. Comparison of efficacy between anti-vascular endothelial growth factor (VEGF) and laser treatment in Type-1 and threshold retinopathy of prematurity (ROP). BMC Ophthalmol. 2018;18(1):19. doi: 10.1186/s12886-018-0685-6 pmid: 29378530
13. Abri Aghdam K, Khadamy J, Falavarjani KG, Tsui I. Refractive outcomes following the treatment of retinopathy of prematurity in the anti-VEGF era: a literature review. J AAPOS. 2016;20(6):539-540.e3. doi: 10.1016/j.jaapos.2016.09.013 pmid: 27810419
14. Tsiropoulos GN, Seliniotaki AK, Haidich AB, Ziakas N, Mataftsi A. Comparison of adverse events between intravitreal anti-VEGF and laser photocoagulation for treatment-requiring retinopathy of prematurity: a systematic review. Int Ophthalmol. 2022. doi: 10.1007/s10792-022-02480-6 pmid: 36214992
15. Chow SC, Lam PY, Lam WC, Fung NSK. The role of anti-vascular endothelial growth factor in treatment of retinopathy of prematurity-a current review. Eye (Lond). 2022;36(8):1532-1545. doi: 10.1038/s41433-021-01922-2 pmid: 35017699
16. Isaac M, Mireskandari K, Tehrani N. Treatment of type 1 retinopathy of prematurity with bevacizumab versus laser. J AAPOS. 2015;19(2):140-4. doi: 10.1016/j.jaapos.2015.01.009 pmid: 25892041
17. Gaber R, Sorour OA, Sharaf AF, Saad HA. Incidence and Risk Factors for Retinopathy of Prematurity (ROP) in Biggest Neonatal Intensive Care Unit in Itay Elbaroud City, Behera Province, Egypt. Clin Ophthalmol. 2021;15:3467-3471. doi: 10.2147/OPTH.S324614 pmid: 34429578
18. Shah VA, Yeo CL, Ling YL, Ho LY. Incidence, risk factors of retinopathy of prematurity among very low birth weight infants in Singapore. Ann Acad Med Singap. 2005;34(2):169-78. pmid: 15827664

19. Etezad Razavi M, Shoeibi N, Hassanzadeh S, Kianmehr S, Bakhtiari E. Refractive outcome of intravitreal bevacizumab injection in comparison to spontaneous regression of retinopathy of prematurity (ROP). Strabismus. 2020;28(1):49-54. doi: 10.1080/09273972.2019.1697302 pmid: 31790628
20. Gundlach BS, Kokhanov A, Altendahl M, Suh SY, Fung S, Demer J, et al. Real-World Visual Outcomes of Laser and Anti-VEGF Treatments for Retinopathy of Prematurity. Am J Ophthalmol. 2022;238:86-96. doi: 10.1016/j.ajo.2021.11.015 pmid: 34788594
21. Geloneck MM, Chuang AZ, Clark WL, Hunt MG, Norman AA, Packwood EA, et al; BEAT-ROP Cooperative Group. Refractive outcomes following bevacizumab monotherapy compared with conventional laser treatment: a randomized clinical trial. JAMA Ophthalmol. 2014;132(11):1327-33. doi: 10.1001/jamaophthalmol.2014.2772 pmid: 25103848
22. 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(6):1119-1124.e1. doi: 10.1016/j.ajo.2013.01.014 pmid: 23490192
23. Mueller B, Salchow DJ, Waffenschmidt E, Joussen AM, Schmalisch G, Czernik C, et al. Treatment of type I ROP with intravitreal bevacizumab or laser photocoagulation according to retinal zone. Br J Ophthalmol. 2017;101(3):365-370. doi: 10.1136/bjophthalmol-2016-308375 pmid: 27301450
24. Adams GG, Bunce C, Xing W, Butler L, Long V, Reddy A, et al; UK Retinopathy of Prematurity Special Interest Group. Retinopathy of prematurity in the United Kingdom: retreatment rates, visual and structural 1-year outcomes. Eye (Lond). 2018;32(11):1752-1759. doi: 10.1038/s41433-018-0151-y pmid: 30013158
25. Kimyon S, Mete A. Comparison of Bevacizumab and Ranibizumab in the Treatment of Type 1 Retinopathy of Prematurity Affecting Zone 1. Ophthalmologica. 2018;240(2):99-105. doi: 10.1159/000489023 pmid: 29920490
26. Chen YC, Chen SN, Yang BC, Lee KH, Chuang CC, Cheng CY. Refractive and Biometric Outcomes in Patients with Retinopathy of Prematurity Treated with Intravitreal Injection of Ranibizumab as Compared with Bevacizumab: A Clinical Study of Correction at Three Years of Age. J Ophthalmol. 2018;2018:4565216. doi: 10.1155/2018/4565216 pmid: 29713524
27. Lin CJ, Tsai YY. Axial length, refraction, and retinal vascularization 1 year after ranibizumab or bevacizumab treatment for retinopathy of prematurity. Clin Ophthalmol. 2016;10:1323-7. doi: 10.2147/OPTH.S110717 pmid: 27499611
28. Hoppe C, Holt DG, Arnold BF, Thinda S, Padmanabhan SP, Oatts JT. Structural and refractive outcomes of intravitreal ranibizumab followed by laser photocoagulation for type 1 retinopathy of prematurity. J AAPOS. 2022;26(6):305.e1-305.e6. doi: 10.1016/j.jaapos.2022.08.524 pmid: 36265750
29. Bayramoglu SE, Sayin N. Factors associated with refractive outcome in children treated with bevacizumab for retinopathy of prematurity: the importance of retinal vascularization. Int Ophthalmol. 2022;42(10):3199-3210. doi: 10.1007/s10792-022-02321-6 pmid: 35579771
30. Vujanović MS, Stanković-Babić GL, Oros A, Zlatanović GD, Jovanović P, Cekić SP, et al. Refractive errors in premature infants with retinopathy of prematurity after anti-vascular endothelial growth factor (anti-VEGF) therapy. Vojnosanitetski pregled. 2017;74(4):323-8. doi: 10.2298/VSP150831191V
31. 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(4):667-74. doi: 10.1097/IAE.0000000000000380 pmid: 25462435
32. 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(1):150-158.e1. doi: 10.1016/j.ajo.2012.06.010 pmid: 22967867
33. Martínez-Castellanos MA, Schwartz S, Hernández-Rojas ML, Kon-Jara VA, García-Aguirre G, Guerrero-Naranjo JL, et al. Long-term effect of antiangiogenic therapy for retinopathy of prematurity up to 5 years of follow-up. Retina. 2013;33(2):329-38. doi: 10.1097/IAE.0b013e318275394a pmid: 23099498
34. Gangwe AB, Agrawal D, Gangrade AK, Parchand SM, Agrawal D, Azad RV. Outcomes of early versus deferred laser after intravitreal ranibizumab in aggressive posterior retinopathy of prematurity. Indian J Ophthalmol. 2021;69(8):2171-2176. doi: 10.4103/ijo.IJO_3016_20 pmid: 34304203
35. Araz-Ersan B, Kir N, Tuncer S, Aydinoglu-Candan O, Yildiz-Inec D, Akdogan B, et al. Preliminary anatomical and neurodevelopmental outcomes of intravitreal bevacizumab as adjunctive treatment for retinopathy of prematurity. Curr Eye Res. 2015;40(6):585-91. doi: 10.3109/02713683.2014.941070 pmid: 25025864
36. Kang HG, Choi EY, Byeon SH, Kim SS, Koh HJ, Lee SC, et al. Intravitreal ranibizumab versus laser photocoagulation for retinopathy of prematurity: efficacy, anatomical outcomes and safety. Br J Ophthalmol. 2019;103(9):1332-1336. doi: 10.1136/bjophthalmol-2018-312272 pmid: 30514709
37. Lee YS, See LC, Chang SH, Wang NK, Hwang YS, Lai CC, et al. Macular Structures, Optical Components, and Visual Acuity in Preschool Children after Intravitreal Bevacizumab or Laser Treatment. Am J Ophthalmol. 2018;192:20-30. doi: 10.1016/j.ajo.2018.05.002 pmid: 29753851
38. Roohipoor R, Karkhaneh R, Riazi-Esfahani M, Dastjani Farahani A, Khodabandeh A, Ebrahimi Adib N, et al. Comparison of Intravitreal Bevacizumab and Laser Photocoagulation in the Treatment of Retinopathy of Prematurity. Ophthalmol Retina. 2018;2(9):942-948. doi: 10.1016/j.oret.2018.01.017 pmid: 31047228
39. O'Keeffe N, Murphy J, O'Keefe M, Lanigan B. Bevacizumab compared with diode laser in stage 3 posterior retinopathy of prematurity: A 5 year follow up. Ir Med J. 2016;109(2):355. pmid: 27685689
40. Gunay M, Celik G, Gunay BO, Aktas A, Karatekin G, Ovali F. Evaluation of 2-year outcomes following intravitreal bevacizumab (IVB) for aggressive posterior retinopathy of prematurity. Arq Bras Oftalmol. 2015;78(5):300-4. doi: 10.5935/0004-2749.20150079 pmid: 26466229
41. 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(5):1008-15. doi: 10.1016/j.ophtha.2014.12.017 pmid: 25687024
42. 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(9):1080-6; quiz 1087. doi: 10.1038/eye.2014.172. pmid:

25104736

43. Harder BC, von Baltz S, Schlichtenbrede FC, Jonas JB. Early refractive outcome after intravitreous bevacizumab for retinopathy of prematurity. Arch Ophthalmol. 2012;130(6):800-1. doi: 10.1001/archophthalmol.2012.1 pmid: 22801850
44. Kang HG, Kim TY, Han J, Han SH. Refractive Outcomes of 4-Year-old Children after Intravitreal Anti-vascular Endothelial Growth Factor versus Laser Photocoagulation for Retinopathy of Prematurity. Korean J Ophthalmol. 2019;33(3):272-278. doi: 10.3341/kjo.2019.0011 pmid: 31179659
45. Roohipoor R, Torabi H, Karkhaneh R, Riazi-Eafahani M. Comparison of intravitreal bevacizumab injection and laser photocoagulation for type 1 zone II retinopathy of prematurity. J Curr Ophthalmol. 2018;31(1):61-65. doi: 10.1016/j.joco.2018.10.008 pmid: 30899848
46. Kabataş EU, Kurtul BE, Altıaylık Özer P, Kabataş N. Comparison of Intravitreal Bevacizumab, Intravitreal Ranibizumab and Laser Photocoagulation for Treatment of Type 1 Retinopathy of Prematurity in Turkish Preterm Children. Curr Eye Res. 2017;42(7):1054-1058. doi: 10.1080/02713683.2016.1264607 pmid: 28128986
47. Gunay M, Sukgen EA, Celik G, Kocluk Y. Comparison of Bevacizumab, Ranibizumab, and Laser Photocoagulation in the Treatment of Retinopathy of Prematurity in Turkey. Curr Eye Res. 2017;42(3):462-469. doi: 10.1080/02713683.2016.1196709 pmid: 27420302
48. 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(2):84-8. doi: 10.3109/09273972.2016.1159232 pmid: 27120579
49. Sahni J, Subhedar NV, Clark D. Treated threshold stage 3 versus spontaneously regressed subthreshold stage 3 retinopathy of prematurity: a study of motility, refractive, and anatomical outcomes at 6 months and 36 months. Br J Ophthalmol. 2005;89(2):154-9. doi: 10.1136/bjo.2004.045815 pmid: 15665344
50. Wong RK, Hubschman S, Tsui I. Reactivation of retinopathy of prematurity after ranibizumab treatment. Retina. 2015(4):675-80. doi: 10.1097/IAE.0000000000000578 pmid: 25768252
51. Hajrasouliha AR, Garcia-Gonzales JM, Shapiro MJ, Yoon H, Blair MP. Reactivation of Retinopathy of Prematurity Three Years After Treatment With Bevacizumab. Ophthalmic Surg Lasers Imaging Retina. 2017;48(3):255-259. doi: 10.3928/23258160-20170301-10 pmid: 28297039