Refractive errors among infants with retinopathy of prematurity who received intravitreal bevacizumab

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ABSTRACT

Aim: To explore the frequency and type of refractive error in eyes that received intravitreal Bevacizumab injection for treatment of retinopathy of prematurity (ROP) and to compare the results with eyes which received intravitreal bevacizumab combined with laser photocoagulation.

Methods: A prospective study conducted at the Ophthalmology Clinic of Queen Rania Al Abdullah Hospital for Children between Jan. 2019 and Oct. 2019. All premature infants who were diagnosed to have severe forms of retinopathy of prematurity and met the threshold to receive intravitreal bevacizumab alone (Group A) or intravitreal Bevacizumab combined with laser photocoagulation (Group B). All patients underwent refraction under cycloplegic effect and the axial length was measured using ultrasound as well. In addition, birth weight, gestational age and result of refraction were recorded. The results of the two groups were compared. All data were analyzed and compared to that obtained in other studies conducted worldwide.

Results: 41 patients (56 eyes) were enrolled in the study; 36 eyes received a single intravitreal bevacizumab of 0.625 mg and 20 eyes received intravitreal bevacizumab combined with laser photocoagulation of the peripheral retina. The frequency of myopia and high myopia was 36% and 8% in group A and 75% and 40% in group B respectively. The axial lengths of both groups were comparable.

Conclusion: In patients with retinopathy of prematurity myopia and high myopia were significantly more frequent in eyes receiving combined intravitreal bevacizumab and laser photocoagulation than in eyes receiving intravitreal bevacizumab alone which was not related to the axial length.

Keywords: Intravitreal bevacizumab, Laser photocoagulation, Myopia, Retinopathy of prematurity

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Introduction

Retinopathy of prematurity (ROP) is vasoproliferative retinopathy that affects the retina of preterm infants leading to the development of neovascularization of the retina and the vitreous (1,2), which eventually causes traction of the retina and detachment.

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(3) ROP is considered as one of the risks for visual morbidity in children and is responsible for around 15% and 60% of the blindness in developed and developing countries respectively. (4) It is well known that vascular endothelial growth factor (VEGF) release in response to retinal ischemia plays a major role in the pathogenesis of ROP. (5) Therefore, the recent addition of anti-VEGF showed to be efficient in minimizing the adverse sequelae of ROP. (7) Previously, cryotherapy and laser photocoagulation of the peripheral retina was mainly used for the treatment of ROP. (8,9)
Laser photocoagulation and to a lesser extent anti-VEGF were reported to be associated with higher incidence of myopia. (10,11) Early detection of refractive errors in children is essential to prevent the development of amblyopia and subsequent probable strabismus. (12)
The aim of the study is to explore the frequency and type of refractive error in eyes that received intravitreal bevacizumab injection for treatment of retinopathy of prematurity and to compare the results with eyes which received intravitreal bevacizumab combined with laser photocoagulation.

METHODS

This prospective study was conducted at the ophthalmology Clinic of Queen Rania Al Abdullah Hospital for Children Jan. 2019 and Oct. 2019. All premature infants who were diagnosed to have severe forms of retinopathy of prematurity and met the threshold to receive intravitreal bevacizumab alone (Group A) or intravitreal bevacizumab combined with laser photocoagulation (Group B) according to the recommendations of the early treatment for ROP study group were included in the study. (13) All patients underwent refraction under cycloplegic effect and the axial length was measured using ultrasound as well. The stage of retinopathy was identified according to the International Classification of ROP. (14) In addition, birth weight, gestational age and result of refraction were recorded. The results from the two groups were compared and all data were analyzed and compared to that obtained in other studies conducted worldwide.

RESULTS

41 patients (56 eyes) meeting the inclusion criteria were enrolled in the study; where,36 eyes received a single intravitreal bevacizumab (Avastin) (IVA) of 0.625 mg (group A) and 20 eyes received intravitreal bevacizumab combined with laser photocoagulation of the peripheral retina (IVAL). The demographic features for group A and B are shown in **Table I**.

Table I: The demographic features of patients

Parameters	Group A patients	Group B patients
Number of eyes	36	20
Gestational age (weeks)	31.3 ± 2.1	29.5 ± 1.1
Birth weight (kg)	1.25 ± 0.25	0.95 ± 0.14
Gender (male percentage)	54%	50%
Age of treatment (estimated GA)	36.2 weeks	33.1 weeks
Normal delivery/Cesarean section	1.2:1	1.3:1

Refraction at 2 years of age in group A ranged between +3.5 D and -8.3 D (mean -1.1 ± 3.9) while the result of refraction in group B ranged between +2.5D and -12.5 D (mean -2.7±4.0).
Table II shows the results of refraction in both groups.

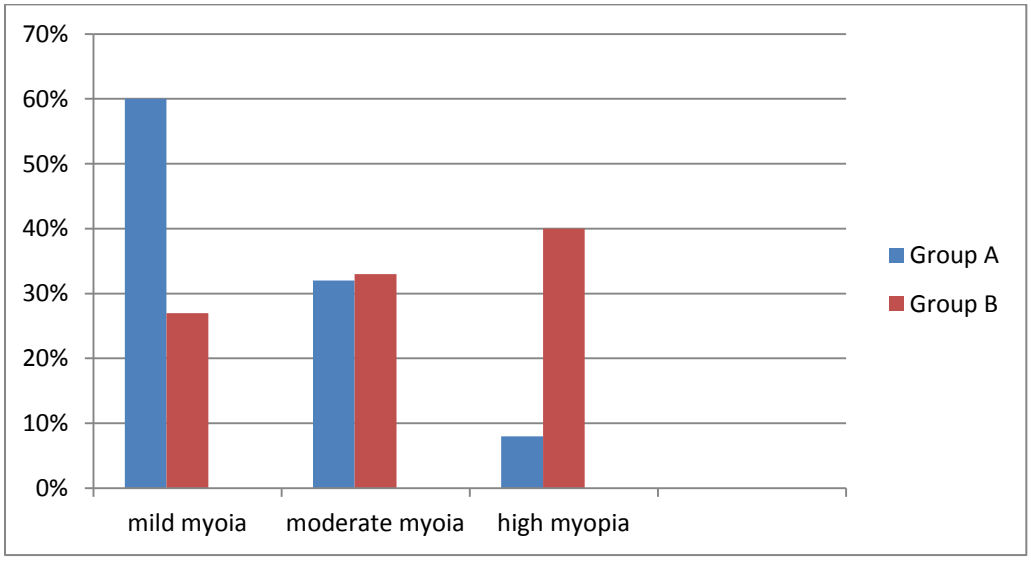
Table II: The outcome of refraction in both groups

Parameters	Group A (36 eyes)	Group B (20 eyes)
Myopia	13 eyes (36%)	15 eyes (75%)
Emmetropia	18 eyes (50%)	3 eyes (15%)
Hyper metropia	5 eyes (14%)	2 eyes (10%)
Astigmatism	10 eyes (28%)	8 eyes (40%)
Axial length (mm)	21.22 ± 1.1	21.31 ± 0.95

Myopia was found in 13 eyes (36%) in group A and 15 eyes (75%) in group B (P value <0.05). Myopia is considered to be mild when it ranges between -0.5 D and -1.5 D, moderate when it is less than -1.5 D and larger than -6.0 D and high when it is less than 6.0 D. (14) **Figure 1** represents the frequency of different degrees of myopia among the two groups. High myopia was much more frequent in eyes that received IVAL (40% of myopic eyes) compared to eyes that received IVA alone (8%) (P value<0.05).

Astigmatism was also more frequent in group B than group A eyes. High astigmatism (more than 1.5 D) was present in 37.5% of astigmatism cases in group B compared with 10% of that in group A. There was no statistical significant difference regarding the axial length between the two groups.

Figure 1, the rates and degrees of myopia in both groups



DISCUSSION

A lot of studies presented evidence regarding the promising effect of intravitreal bevacizumab and laser photocoagulation in the treatment of ROP. (15) In Jordan, there is no doubt that those measures greatly contribute to the regression of the disease and improve the prognosis. Many researchers talked about the higher prevalence of refractive errors among premature infants particularly after treatment with IVA, laser photocoagulation, cryotherapy and vitrectomy with variable percentages. (16) Early detection of refractive errors in children is essential to prevent permanent deterioration of vision which may result from amblyopia if left untreated. (17)

In this study refractive errors were present in eyes that received IVA or IVAL with variable percentage. Myopia and high myopia were the most frequent finding in eyes with IVA. Martinez et al found that the frequency of myopia and high myopia were 55.6% and 11.1% among eyes that received intravitreal bevacizumab alone respectively. (18) In our study also a higher frequency of myopia and high myopia approaching 36% and 8% respectively were seen when compared to other studies which explored the frequency of refractive errors particularly myopia in premature infants with or without ROP. (19) In eyes, with IVAL the frequency of myopia and high myopia was also high approaching 75% and 40%. Chen et al found that the frequency of myopia and high myopia to be 82.4% and 29.4% respectively. (16) When the results of the two groups are compared it is clearly observed that the frequency of myopia and high myopia is significantly more in eyes with IVAL compared to eyes with IVA, this was a common finding in studies with a similar method of conduction. (16,20) Myopia can be caused by either increased axial length or anterior segment abnormality; this study showed comparable results of axial length between the two groups which suggests that myopia was more related to anterior segment abnormality rather than increase axial length. Researchers reported that eyes with ROP have steeper corneal curvatures, shallower anterior chamber depths, greater lens thicknesses, and increased macular thicknesses which will contribute to the development of myopia. (21) There is a lot of controversy regarding the explanation of myopia development and its severity whether is it related to the severity of ROP or due to the type of treatment offered for ROP. (16,22) However, it should be considered that the choice of treatment of ROP depends on the grade and severity of ROP.

The current study also showed a higher frequency of astigmatism in eyes receiving IVA and IVAL being slightly more in the later. Previous studies reported a higher frequency of astigmatism among ROP children.

Further studies are needed to explore the prevalence of astigmatism in premature infants with or without ROP and with or without treatment.

This study was limited due to the small size of the sample and the relatively short duration of follow up which was mainly related to the loss of follow up of patients at our clinic after receiving treatment. However, this study showed the significant high frequency of myopia and high myopia among eyes receiving combined intravitreal bevacizumab and Laser photocoagulation than eyes receiving intravitreal bevacizumab alone which was not related to the axial length.

CONCLUSION

In patients with retinopathy of prematurity myopia and high myopia were significantly more frequent in eyes receiving combined intravitreal bevacizumab and laser photocoagulation than in eyes receiving intravitreal bevacizumab alone which was not related to the axial length.

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