Letter to the Editor

The battle between photocoagulation and antiVEGFs in Retinopathy of Prematurity and the road ahead

Gunjan Prasai[1], Sabina Shrestha[1]
[1]Kathmandu Medical College, Sinamangal, Kathmandu, Nepal

Key words: Retinopathy of Prematurity, Laser photocoagulation, Bevacizumab, Ranibizumab

The Editor-in-Chief,

Nepalese Journal of Ophthalmology,

Nepal

We were intrigued to read the review article- Bevacizumab in Retinopathy of Prematurity: Concerns and adverse effects (Sharma, A., Shetty, A., & Reddy, Y. V. G. (2020). They have admirably highlighted the benefits of using Bevacizumab in preterm infants presenting with retinopathy of prematurity (ROP) as opposed to laser photocoagulation. With increasing preterm infants' survival due to availability of better health facilities in developed as well as developing countries, this article appeared very judicious. We would like to congratulate the authors for this successful review article, and make some contributions.

Financial Interest: Nil
Conflict of Interest: Nil
Received: Accepted:

Corresponding author
Dr Gunjan Prasai
Kathmandu Medical College, Sinamangal, Kathmandu, Nepal
E-mail: prasaigunjan@gmail.com

Access this article online
Website: www.nepjol.info/index.php/NEPJOPH

DOI: https://doi.org/10.3126/nepjoph.v13i1.30652

ISSN: 2072-6805, E-ISSN: 2091-0320

Although laser photocoagulation of the avascular retina remains a viable option for the patients that cannot present for regular follow-ups, the irreversible destruction of the retinal tissue; eventual constriction of peripheral vascular field; increased incidence of myopia and longer duration of sedation for the procedure with lasers make anti –Vascular Endothelial Growth Factors (anti-VEGFs) a more agreeable treatment modality. Laser photocoagulation also further destroys the natural retinal barriers in an eye with an already compromised blood retinal barrier. Hence, it is more sensible to use Bevacizumab as the first line therapy and not after the failure of laser treatment (Nicoars et al., 2015).

Anti-VEGFs like Bevacizumab are less vicious and more directed towards the pathogenesis of retinopathy of prematurity (ROP). Nonetheless, despite numerous studies a definite management protocol for ROP using antiVEGFs and their long term safety has not been established. Trials have been conducted starting with a higher dose so as not to undertreat this potentially blinding disease and went on decreasing the dose until adequate regression of disease was seen with complete retinal vascularization and without any recurrence for up to 60- 72 weeks (Fouzdar Jain *et al.*, 2018). The minimum efficacious dose of Bevacizumab was found to be 0.004 mg by Wallace et. al. in a National Eye Institute (NEI) - funded Pediatric Eye Disease

Investigator Group (PEDIG) study (Wallace et al., 2020).

The side effects associated with anti-VEGF injections have been recorded as tractional retinal detachment, endophthalmitis, vitreous hemorrhage, myopia, prolonged time for retinal maturity, pulmonary hypoplasia, stroke, developmental delay and death even up to twelve months later. (Fouzdar Jain et al). We must also be cautious that reactivation of ROP may occur after Bevacizumab at the posterior site with extraretinal fibrovascular proliferation and not at the junction of the avascular and vascular retina. Thus, the follow- up duration should be kept more frequent and intense. (Hittner-Mintz HA et al., 2011)

Another important thing we must keep in mind is that VEGF is required for neural survival also so prolonged suppression of VEGFs can hamper the physiological development of neural retinal constituents. (Nicoars. S.D. et al, 2015) Ranibizumab has a higher affinity with VEGF with a shorter half-life than Bevacizumab thus having more efficacy, less systemic absorption and early clearance. Systemic VEGF levels have been found to decrease at 2-3 weeks and return to normal levels at 4 weeks with Ranibizumab whereas the systemic levels remain decreased for up to 2 months with Bevacizumab. Hence, Ranibizumab was started to be used on neonates suffering with ROP. However, response on the contralateral eye on unilateral injection has been observed with both of these drugs. (Wong, Hubschman and Tsui, 2015)

So, in spite of more widespread off label use of Bevacizumab for the treatment of ROP, Ranibizumab was the first licensed pharmacological alternative for laser photocoagulation for the treatment of ROP. This happened thanks to the RAINBOW study (Ranibizumab versus laser therapy for the treatment of very low birth weight infants with retinopathy of prematurity) which showed that only 0.2mg of Ranibizumab was safer and more efficacious than lasers with a 24 week safety profile. (Menke et al., 2015).

For years lasers remained the backbone of treatment for ROP but down the years, the many adverse events as mentioned above deemed a necessity for an alternative. Though anti- VEGFs seem the sensible substitute for now, their use is still in its incipient stage and the long term effects are yet to be seen to completely replace lasers as the main modality of therapy for ROP.

References

Fouzdar Jain, S. et al. (2018) 'Retinopathy of prematurity: Preferred practice patterns among pediatric ophthalmologists', Clinical Ophthalmology, 12, pp. 1003–1009. doi: 10.2147/OPTH.S161504.

Menke, M. N. et al. (2015) 'Intravitreal ranibizumab monotherapy to treat retinopathy of prematurity zone II, stage 3 with plus disease', BMC Ophthalmology, 15(1), pp. 1–6. doi: 10.1186/s12886-015-0001-7.

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.

Nicoarə, S. D. et al. (2015) 'Outcomes and Prognostic Factors of Intravitreal Bevacizumab Monotherapy in Zone i Stage 3+ and Aggressive Posterior Retinopathy of Prematurity', Journal of Ophthalmology, 2015. doi: 10.1155/2015/102582.

Wallace, D. K. et al. (2020) 'Short-term Outcomes after Very Low-Dose Intravitreous Bevacizumab for Retinopathy of Prematurity', JAMA Ophthalmology, 138(6), pp. 698–701. doi: 10.1001/jamaophthalmol.2020.0334.

Wong, R. K., Hubschman, S. and Tsui, I. (2015) 'Reactivation of retinopathy of prematurity after ranibizumab treatment', Retina, 35(4), pp. 675–680. doi: 10.1097/IAE.0000000000000578.