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Effect of Intravitreal Bevacizumab on macular edema secondary to retinal vascular occlusion

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Abstract
Objective: To find out the effect of intravitreal injection of Bevacizumab on central macular thickness (CMT) and best corrected visual acuity (BCVA) in cases of retinal vascular occlusion (RVO).
Material and method: All the patients of RVO treated at our institute over a period of 1 year, with a central macular thickness of more than 250µ were included in the study. Intravitreal injection of Bevacizumab was given and the CMT and BCVA were measured after a control period of 1 month. The injection was repeated at intervals of 1.5 months if decrease in CMT was less than 30%.
Result: Out of the total 78 patients there was a significant improvement in BCVAin 58 patients. There was a significant decrease in central macular thickness in all of them.
Conclusion: Anti-VEGF agent Bevacizumab causes significant reduction in central macular thickness and improves BCVA in cases of macular edema secondary to retinal vascular occlusion.

Keywords: Macular edema, retinal vascular occlusion, anti-VEGF, intra-vitreal injection, central macular thickness, best corrected visual acuity

Introduction
Retinal vascular occlusion (RVO) is an important retinal vascular disorder, second only to diabetic retinopathy in prevalence. It is associated with various risk factors such as age, hypertension and co-existing cardio-vascular disorders [1]. Macular edema is a major cause of loss of vision in both branched retinal vein occlusion and central retinal vein occlusion, accounting for 5-15% cases in former and almost all cases in latter [2]. While observation is recommended for cases having visual acuity 6/9 or better, grid laser had been used if visual acuity is 6/12 or worse to treat macular edema. But over the recent years intravitreal anti-VEGF (anti-Vascular Endotheial Growth Factor) agents have been widely adopted for this purpose, apparently raising acuity more than laser [2]. In our study we evaluate the effect of intravitreal Bevacizumab on BCVA and central macular thickness in RVO patients over a period of 1 year. In order to reduce the financial and logistical burden we used one injection and pro re nata regimen.

Materials and Method
Patients being treated for RVO at our institute between 1st June 2017 to 31st May 2018 were included in the study.
Inclusion criteria:
- Patients having worsening of visual acuity over last 6 months of worsening of disease
- Central macular thickness ≥ 250µ on OCT
- Exclusion criteria:
- Macular edema due to other cause (eg, diabetic retinopathy)
- Significant media opacity (eg, cataract)
- Some other eye surgery in previous 6 months
- Previously treated with intravitreal anti-VEGF or Laser photocoagulation.

After taking proper history about the duration of occlusion and presence of other systemic diseases, BCVA was recorded using Snellen's chart and central macular thickness was noted using OCT. Anterior and posterior segment examinations were done, the characteristics of occlusion and other fundus findings were noted. Intra-vitreal injection of 1.25mg/0.05ml Bevacizumab was administered. BCVA, and presence of any infection were noted after 1 week. After a control period of 1 month, BCVA and CMT were compared with the pre-

pre-operative result. In patients having an improvement in BCVA and decrease in CMT of >30% further injections were given depending on anatomical and functional results and physician discretion, while in those with <30% improvement two more injections were given at 1.5 months interval. BCVA, IOP and CMT were documented at 3 months, 6 months and 1 year.

Results

78 eyes of 78 patients were examined. Mean age was 56.38±11.23 years (23-86yrs) and 41(52.56%) were men and 37(47.44%) women.27 eyes had CRVO while 51 had BRVO. Accordingly 46 patients received 1 injection, 22 received two while 10 got ≥3 injections. There was clinically significant improvement in BCVA (>3.0logMAR units) in 58 patients, while in 20 patients it wasn't significant (<3.0logMAR units).BCVA improved from 1.36±0.76 logMAR units to 0.63±0.2 logMAR units at 1 year post-op in CRVO patients while it improved from 0.85±0.32 logMAR units to 0.34±0.4 logMAR units in BRVO patients.

	CRVO	BRVO	Total
Eyes with significant improvement in BCVA	14	44	58
Eyes without any significant improvement in BCVA	13	7	20
Total	27	51	

Central macular thickness (CMT) decreased significantly from 847.36±237.28µ at baseline to 298.76±213.34µ at 1 year post-op in CRVO patients whereas in BRVO patients it decreased from 538.43±206.56µ to 276.74±199.83µ. No significant change in IOP was noted in both the groups at the end of 1 years.

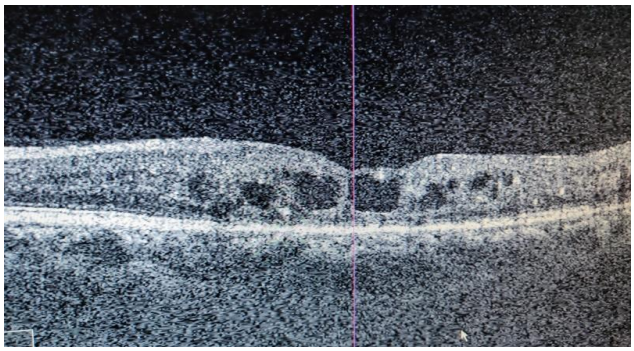

Fig 1: OCT image of a case of BRVO before injecting intravitreal Bevacizumab

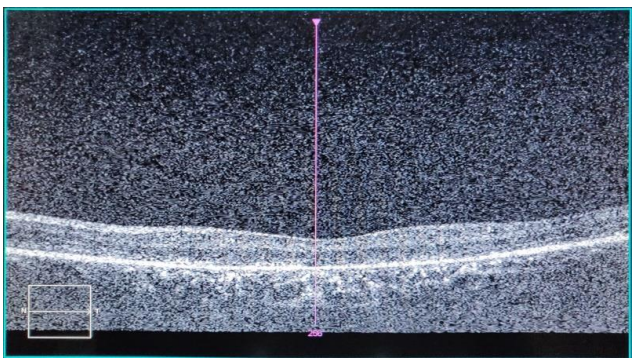

Fig 2: OCT image of the same patient after Bevacizumab injection and 1 year follow-up

A group of 29 patients who refused treatment were also followed up for 1 year. Although they showed a significant decrease in CMT but improvement in BCVA wasn't significant. So, patient receiving intravitreal injection had significantly better BCVA at the end of 1 year for both CRVO and BRVO cases as compared to controls, while there was no significant difference in CMT. The case and control groups were confounded for various independent variables like, duration of disease, hypertension, diabetes mellitus, hyperlipidemia and systemic thrombosis.

Discussion

Various modalities have been in use to treat macular edema caused by retinal vascular occlusion. Focal or grid laser and sector phocoagulation are used specially when macular ischemia is present. Intravitreal Dexamethasone implant has resulted in significant improvement of vision but it is associated with adverse effects like increased risk of cataract and glaucoma. Intravitreal Triamcinolone is as effective as laser in reducing macular edema but has less sustained effect. It is also associated with increased risk of cataract formation and IOP elevation. Periocular steroids have also been used but they are less efficacious than injections Various studies have been previously conducted to evaluate the efficacy of intravitreal anti-VEGF injections in reducing macular edema in retinal vaso-occlusion. Most of these studies (Hikichi *et al*, Epstein *et al*) [3, 4] have shown significant improvement in BCVA and reduction in CMT with intravitreal Bevacizumab, quite comparable to our study. Two large studies (BRAVO and CRUISE) [5, 6] got similar results with Ranibizumab. Another randomized trial (MARVEL) [7] carried out to compare the results of Bevacizumab and Ranibizumab found them mostly similar. There have been no systemic adverse effects with the use of these agents

Conclusion

Anti-VEGF agents have been proved to be quite effective in treating macular edema secondary to retinal vascular disease. In our study this has been demonstrated by use of low dose intravitreal Bevacizumab. Further studies need to be done to evaluate the long term continuity of anatomical and functional recovery.

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