

Comparison of Effectiveness & Complications of Bevacizumab & Triamcetonolone Acetonide, in the Treatment of Macular Edema Secondary to Branch Retinal Vein Occlusion

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ABSTRACT

Objective: To evaluate the magnitude of improvement in vision after Intra-Vitreous Bevacizumab (IVB) and intra-vitreous Triamcetonolone acetonide (IVTA) injection in Branch Retinal Vein Occlusion (BRVO).

Study design: Comparative case series study

Place and Duration: Department of Ophthalmology, Al-Ibrahim Hospital and Al-Tibri Medical College Hospital from April 2013 to October 2013.

Subjects and Methods: 32 patients (32 eyes) of BRVO were included in the study using Non-probability purposive sampling according to the inclusion and exclusion criteria. Informed written consent was taken. Baseline vision (BCVA) was noted using Early Treatment of Diabetic Retinopathy Study (ETDRS) acuity chart. Central macular thickness (CMT) was computed using optical coherence tomography (OCT). Patients were randomly allocated into 2; Group A (Becavizumab, n=18) and Group B (Triamcetonolone acetonide, n=14). Visual findings and central macular thickness of last follow-up (8weeks) was analyzed. The data was analyzed on *SPSS 21.0 version* using student t-test and Chi square test. A p-value of = 0.05 was taken statistically significant.

Results: Of 32 eyes, 18 eyes (56.3 %) were given intra-vitreous injection of Becavizumab while 14 (43.8%) received intra-vitreous triamcetonolone. No differences were observed in BCVA for distance (p=0.76) and near (p=0.95) between the groups at second follow up (after 4 weeks). Mean central macular thickness was less in group B compared to Group A but the difference was not statistically significant (p=0.23). Subconjunctival hemorrhage, raised IOP and cataract were the complications observed.

Conclusion: Triamcetonolone is as effective as Becavizumab in visual improvement due to macular edema secondary to Branch Retinal Vein Occlusion. Also, it causes almost similar reduction in Central macular thickness compared to Becavizumab.

Key words: Becavizumab, BRVO, Macular edema, Triamcinolone acetonide, visual acuity

INTRODUCTION

Branch retinal vein occlusion (BRVO) is a visually disabling condition. The incidence of the disease in population of 40 years and above is

2.14/1000/year.¹ Few studies in past has shown that BRVO predisposes to increased levels of Vascular Endothelial Growth factor, which causes macular edema².

Branch retinal vein occlusion involves one of the branch retinal veins. It's incidence in an outpatient referral setting is roughly the same as that of central retinal vein occlusion.³ The occlusion of a macular vein is a distinct entity that is discussed separately⁴.

BRVO very rarely involves temporal branches. Whether this is because the incidence is truly rare or because these occlusions are generally asymptomatic and discovered only incidentally is unknown⁵. Occasionally a branch retinal vein

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occlusion occurs nasally and involves the entire nasal retina.

Previously photocoagulation has been used as a treatment modality for macular edema but it resulted in limited success. Similarly triamcnenolone has been used which has shown variable success but at the expense of higher rate of complications.^{2,3} Recently, another modality has been very widely used, which is Bevacizumab. It causes both reductions in macular edema as well as improvement in vision.⁶ It is a monoclonal antibody against the Vascular endothelial growth factor. Its molecular weight is 142 kD. It works basically by binding to all isoforms of vascular endothelial growth factor and thus inhibiting its effects and reducing not only the neovascularization but also macular/retinal edema.⁷

Triamcnenolone acetonide on the other hand is effective in reducing macular edema but has the biggest advantage of being cost effective treatment but at the expense of higher frequency of complications.⁸ Thus this gives us the opportunity to compare the two treatment options head to head with each other in order to confirm whether these are effective in reducing the macular edema or not if yes than which of the two is more effective and also compare the consequences of the two drugs in terms of side effects⁹. Therefore, the purpose of present study was designed to investigate the effects of Bevacizumab and Triamcnenolone acetonide in branch retinal vein occlusion at our tertiary care hospital.

MATERIAL & METHODS:

The present comparative case series study was conducted at the Department of Ophthalmology, Al-Ibrahim Eye Hospital and Al-Tibri Medical College Hospital from April 2013 to October 2013. A sample of 32 patients (32 eyes) of BRVO was included in the study using non-probability purposive sampling according to the inclusion and exclusion criteria. Macular edema associated with Branch Retinal Vein Occlusion. Macular Edemas deemed positive when macula looks thicker than the rest of the retina, examined by an ophthalmologist with at least 2 years postgraduate experience with slit lamp

biomicroscope and 90 diopter lens. Branch Retinal Vein Occlusion was deemed as present when multiple flame-shaped hemorrhages were present in any quadrant of the fundus associated with dilated retinal vein. Retinal vein was considered as dilated when its caliber is larger than the rest of the veins of the fundus examined by an ophthalmologist with at least 2 years postgraduate experience with slit lamp biomicroscope and 90 diopter lens) of either gender. BRVO associated with severe complications, tractional Retinal detachment, Vitreous hemorrhage, Macular pucker, Glaucoma, macular edema of other causes such as age related maculopathy, diabetic maculopathy and central retinal vein occlusion (CRVO) were excluded. Informed written consent was taken. Baseline vision (BCVA) was noted using ETDRS acuity chart. Central macular thickness (CMT) was computed using optical coherence tomography (OCT). Patients were randomly allocated into 2; Group A (Bevacizumab, n=18) and Group B (Triamcnenolone acetonide, n=14). Visual findings and central macular thickness of last follow-up (8 weeks) was analyzed. The data was analyzed on SPSS 21.0 (IBM, incorporation, USA). The continuous variables were analyzed by student t test and presented as mean \pm SD. The categorical variables were analyzed by Chi-square test. A p value of ≤ 0.05 was taken statistically significant.

RESULTS:

Mean age was noted 53.68 ± 9.01) and range of 37 - 80 years. 16 (50%) were male while 16 (50%) were female. Right eye was involved in 16 (50%) of the patients while left eye was involved in 16 (50) of the patients. Mean duration of BRVO was 8.59 months (± 3.29), with minimum duration of BRVO of 4 months and maximum duration of BRVO of 20 months. CMT at baseline was 355.93μ (± 159.73), with minimum central macular thickness of 147μ and maximum central macular thickness of 745μ . No significant difference (p value=0.643) in vision was observed between both the groups. Similarly, no significant difference (p value=0.85) was observed in BCVA for near between the groups at first follow up as well. When we observed the difference in BCVA

for distance and near between the groups at second follow up (after 4 weeks) we again failed to observe any significant difference between the groups. At final follow up again, no statistical significance was seen between the two groups, when BCVA was compared between the two groups (for distance $p = 0.76$ and for near ($p = 0.95$). Although, mean central macular thickness was less in group B compared to Group A but the difference was not statistically significant ($p=0.23$). In Group B, 15 (83%) patients showed visual improvement compared to 10 (71.42%) in Group A. 2 patients showed decrease vision in either group. On the other hand, 3 patients (1 in group B and 2 in group A) showed neither improvement nor decrease in vision on comparison of pre and post treatment vision. Procedure related complications such as subconjunctival hemorrhage was seen in both groups but slightly higher in IVTA group ($p=0.621$). Similarly another complication probably due to procedure was endophthalmitis, which was seen in single patient. Other complications noted were raised IOP and cataract. Cataract was seen only in one patient of IVTA group but till the study follow up period it was not causing significant visual distortion. On the other hand, raised IOP was noted in 4 (22.22%) patients of IVTA group. Mean IOP change was $8.56 \text{ mm Hg} \pm 6.24 \text{ mm Hg}$, with minimum change of 5.89 mm Hg and maximum change of 11.23 mm Hg . IOP of these patients were successfully controlled with topical drugs. Two of the patients received topical Beta blocker while 2 needed combination therapy of topical Beta blocker and dorzolamide. Raised IOP was not observed in IVB group.

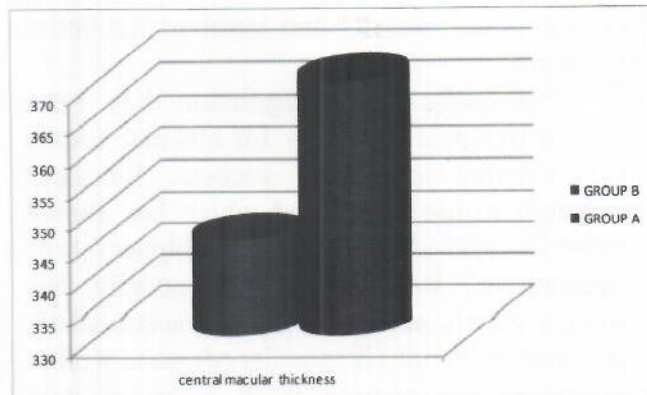


Figure 2: Comparison of Baseline Central Macular Thickness Between Groups

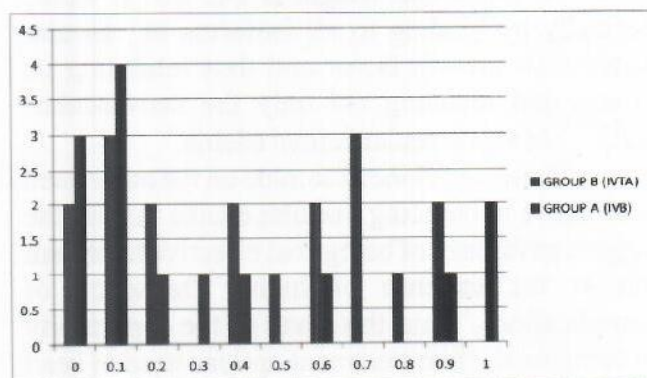


Figure 3: Comparison of BCVA-distance at week 4

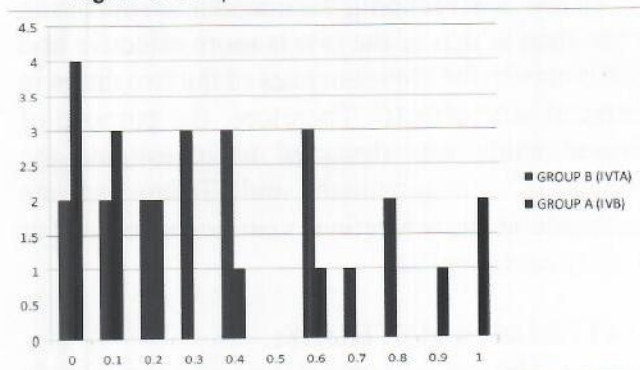


Figure 4: Comparison of BCVA-near at week 4

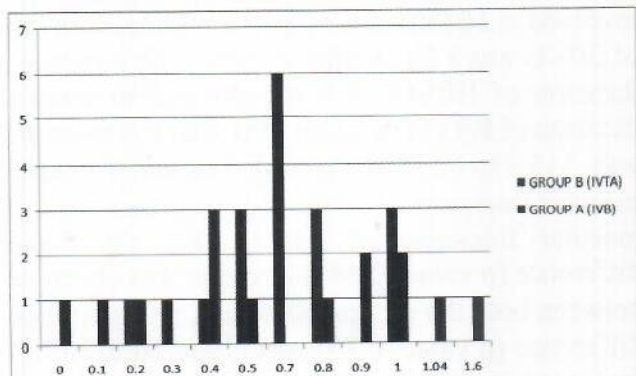


Figure 1: Comparison of Baseline BCVA between Two Groups

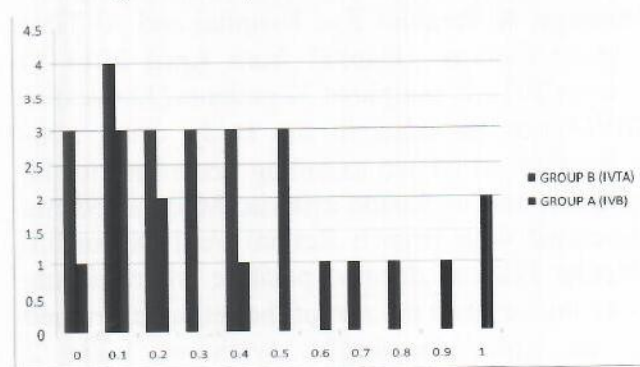


Figure 5: Comparison of BCVA-near at week 8

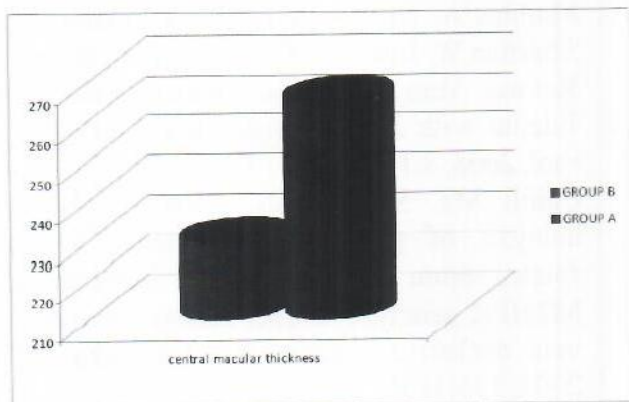


Figure 6: Final Central Macular Thickness between Groups

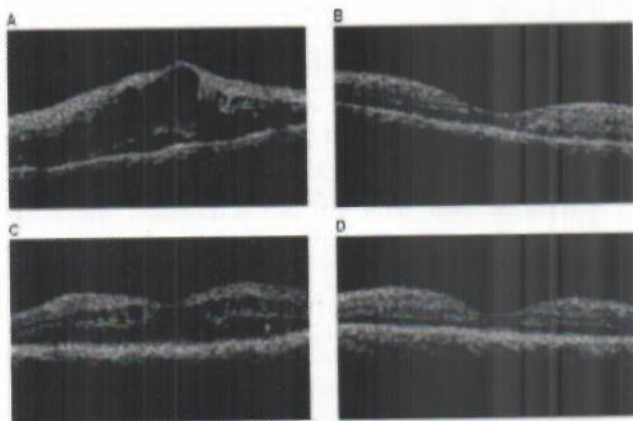


Figure 7: A. Pre-Injection Baseline IVTA
 B. Post-Injection IVTA at week 8
 C. Pre-Injection Baseline IVB
 D. Post-Injection IVB at week 8

DISCUSSION:

Retinal vein occlusion is one of the major causes of blindness worldwide. Still controversies exist in the management options to be preferred one over other.¹ Although, most of the researchers believe that early detection of the disease can prevent vision loss if managed properly and appropriately thus reducing the morbidity.^{2,3} Controversies also exist regarding the exact causes of retinal vein occlusion, but thrombus formation has been considered as the most important cause of retinal vein occlusion.¹⁰ Retinal vein occlusion has been the subject of almost incessant research but still now so many still believe that the etiology and intimate mechanism of obstruction are still unelucidated.¹¹

Branch retinal vein occlusion (BRVO) is one of the frequent retinal vascular diseases seen in

retina clinics.¹² BRVO can cause reduced blood perfusion to retina and ultimately retinal hypoxia resulting in vision loss. It can also be complicated by macular edema. Macular edema caused by retinal vein occlusion will further intensify the vision loss. Some time the vision loss caused by macular edema exceeds the vision loss caused by hypoxia itself. Multiple treatment options have been tried in past by many researcher including laser photocoagulation.^{13,14}

It has been shown in many studies that vascular endothelial growth factor is one of the factors that is released in increased amount after branch retinal vein occlusion and is associated with certain complication such as macular edema.¹⁵ The exact mechanism behind this effect is that the retinal ischemia causes up regulation of vascular endothelial growth factor.

In many studies, IVTA has been used in patients with macular edema secondary to BRVO. Variation has been reported in its success by many researchers.¹⁶

This mechanism made many researchers believe that by inhibiting the vascular endothelial growth factor, vascular leakage could be prevented thus resulting in reduction of macular edema.¹⁵ Another study by Gary Edd Fish, in which they retrospectively analyzed 56 patients with BRVO. These patients had been treated with Bevacizumab alone or combined with Triamcnenolone. The group which received Bevacizumab without Triamcnenolone acetamide had maximum improvement.¹⁷

Badalà in his study also confirmed the effectiveness of Bevacizumab in improving the macular edema due to BRVO. They also reported that 2-3 injections might be needed in every patient due to short half life of the Bevacizumab injection, which the reported to be around 6-7 weeks only.¹⁸

Rabeena studied the effects of Bevacizumab in macular edema due to BRVO.¹⁹ They also reported a highly successful result of Bevacizumab Injections when given intravitreally in not only improving vision but also reducing the central macular thickness as well, with almost negligible adverse effects. Another studies reported similar effectiveness with safety of the drug.^{20,21}

Similar studies were performed on Triamcenolone acetonide as well. They reported its effectiveness and adverse effects such as raised IOP and risk in intraocular infections.^{22,23}

In present study, 83% of the patients who were treated with IVTA patients showed visual improvement compared to 71.42% in patients, treated with Bevacizumab injection intra-vitreally. Although, visual and anatomical success was higher in the IVTA group, but complications were more frequently observed in this group compared to IVB group.

CONCLUSIONS:

Triamcenolone is as effective as Bevacizumab in visual improvement due to macular edema secondary to Branch Retinal Vein Occlusion. Also, it causes almost similar reduction in Central macular thickness compared to Bevacizumab. Effect of Bevacizumab decrease at week 4 onward compared to Triamcenolone. Although, further trials with longer duration and larger sample sizes is needed but this study proves that Intravitreal Triamcenolone is as effective as Bevacizumab in visual improvement and resolution of macular edema in Branch retinal Vein Occlusion.

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