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To Compare Morphological and Visual Acuity Outcomes Associated With Single Intravitreal Injection of Triamcionolone Acetonide versus Bevacizumab for the Treatment of Macular Edema Associted with Retinal Vein Occlusion

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Abstract
Introduction: *Present study was conducted to assess the effect on the morphological and visual acuity outcomes associated with the use of single intravitreal injection of triamcinolone acetonide or with the use of single intravitreal injection of bevacizumab treatment for RVO associated with macular edema.*
Methodology: *This is prospective, randomized and open labeled study conducted on 64 patients of macular edema associated with retinal vein occlusion. All patients were grouped into two groups to receive either single intraviteral injection of 4mg/0.1 ml triamcinolone acetonide or single intravitreal injection 1.25mg/0.05 ml of bevacizumab.*
Results: *There were 64 eyes of 64 patients who at baseline had a mean age of 56.7±9.9 years. A rapid response in visual acuity in both groups that began within few weeks after the first injection with a mean BCVA improvement of 0.323±0.200 and 0.236±0.187 logMAR from baseline at 6 weeks after injections in the IVT and IVB groups respectively. There was significant resolution of ME decreases as measured by OCT within each group postoperatively.*
Conclusion: *This study indicates that intraviteral injections of either TA or bevacizumab can both improve visual acuity and decrease ME in eyes with CRVO.*
Keywords: *Bevacizumab Macular Edema, Retinal Vein Occlusion, Triamcinolone Acetonide*

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I. Introduction

Central retinal vein occlusion (CRVO) is the second-most common disorder after diabetic retinopathy (1). One of the main reasons of vision loss is CRVO in acute and chronic forms. There are many risk factors associated with CRVO including age, hypertension, diabetes mellitus, retinal artery atherosclerotic changes, open-angle glaucoma and hyperopia (2). Its prevalence increases with age and varies from 0.1% to 5%. Visual acuity is a reflection of the severity of the disease, retinal macular hemorrhage, cystoid macular edema and ischemia (3). Macular edema is one of the fundamental causes of vision loss in chronic and acute CRVO as well as ischemic and non-ischemic forms (4). CRVO study showed that although the macular network photocoagulation decreased angiographic edema, the vision did not improve (3). Recently, the standard treatment for central retinal vein occlusion was limited to photocoagulation for neovascular adverse effects and there was no solution to macular edema (3). The main trigger for the formation of edema and macular neovascularization in patients with CRVO is the production of vascular endothelial growth factor (VEGF (caused by hypoxia, which is an angiogenic factor, causing angiogenesis and increase of vascular permeability (5). It has been shown that vascular endothelial growth factor increases in eyes with CRVO (6). Some studies, as noted, have shown that the injection IVB and injection of IVT have beneficial effects for these cases. However, due to their half-life, repeated injections are required (7). Studies did not have the same results on the effectiveness and safety of these therapies in CRVO, and so, this shows the importance of this study in the world. Thus, the aim of the study was to compare the effectiveness of IVT and IVB separately and combined, for the treatment of patients with CRVO, to obtain the best choice.

II. Materials And Methods

This is prospective, randomized and open labeled study. This study was conducted on 64 patients of macular edema associated with retinal vein occlusion.

Inclusion criteria: 1) best –corrected visual acuity (BCAV) worse than 20/40 log MAR=0.3, 2) clinically detectable ME involving fovea with thickness of >250mm confirmed by optical coherence tomography, 3) symptomatic duration > 2weeks, 4) no history of previous treatment.

Exclusion criteria: 1) intraocular pressure>21 mm oh Hg, 2) previous intraocular surgery within the past 2 years, 3) grid photocoagulation for ME, 4) previous intraocular use of AT or anti-VEGF drugs, 4) coexistence of uncontrolled hypertension or diabetes mellitus etc., 5) presence of IRIS neovascularization, 6) OCT evidence of a vitreoretinal interface abnormality and ocular morbidity such as uveitis, glaucoma, or vitreoretinal disease. All patients were grouped into two groups to receive either single intraviteral injection of 4mg/0.1 ml triamcinolone acetonide or single intravitreal injection 1.25mg/0.05 ml of bevacizumab. Statistical analysis was done using SPSS version 16.0.1. Statistical significant were set at p-value <0.05.

III. Results and Discussion

Macular Edema (ME) represents an important vision threatening complications of CRVO. Patients with CVO report difficulty with many aspects of daily life and have decreased vision-related quality of life as measured by the 25 item National eye Institute Visual Function Questionnaire 1.

Some studies compared the resolution of ME and BCVA and found that therapeutic effects of IVT showed no significant differences as compared with IVB regarding anatomical and functional outcomes. Only bevacizumab was devoid of unfavorable IOP elevations (8) (18-21).

This is a prospective intervention study evaluating the efficacy and safety outcomes of IVT and IVB treatment for ME secondary to CRVO. There were 64 eyes of 64 patients who at baseline had a mean age of 56.7±9.9 years.

We report our six weeks follow-up results with treatment of IVT and IVB in patients with ME because of CRVO.

Our study found a rapid response in visual acuity in both groups that began within few weeks after the first injection with a mean BCVA improvement of 0.323±0.200 and 0.236±0.187 log MAR from baseline at 6 weeks after injections in the IVT and IVB groups respectively (Table: 1). The patients continued to show improvement with 87.5% and 75% having improvement in acuity at the final visit. The IVT group seems to have achieved more character than that in the IVB group, although without significant difference, which was possibly because of the limited sample size in the study.

Table: 1 Comparison of Visual Acuity between IVT and IVB groups.

	IVT Group	**IVB Group**	**P-value**
Number of injection	1	1	
BCVA (Mean±SD) logMAR			
Baseline	1.136±0.443	0.96989±0.3516	0.248
1st week	0.9455±0.4750	0.8681±0.370	0.512
6 weeks	0.81294±0.5059	0.73338±0.3210	0.599
Improvement of post-injection BCVA (Mean±SD) logMAR			
1st week	-0.1909±0.250	-0.1017±0.218	0.274
6 weeks	-0.323±0.200	-0.236±0.187	0.251

There was significant resolution of ME decreases as measured by OCT within each group postoperatively. Initial mean CMT was 592.6±158.78 µm and got 40.15% resolution at 6 weeks postoperatively in the IVT group, whereas the baseline CMT was 552.6±197.04 µm in the IVB group and got 34.87% resolution at 6 weeks, respectively (Table: 2). Interestingly, the response was more rapid and pronounced in IVT groups 6 weeks postoperatively and the CMT declined dramatically within the first 6 weeks after initial injection. Quamar et al found that the macular thickness of the eyes treated with an IVT injection was significantly reduced after one (222.7±13.4 µm; p<0.001) and three months (228.1±10.6 µm; p<0.001) of treatment. The eyes treated with a PST injection displayed a slow response and a significant improvement in macular thickness that was observed only after three months (231.3±10.9 µm; p<0.001). The difference between the eyes treated with an IVT injection (385.2±11.3 µm) and those treated with a PST injection (235.4±8.7 µm) was significantly different six months after treatment (p<0.001) (9).

Table: 2 Comparison of CMT between IVT and IVB groups.

	IVT Group (n=16)	**IVB Group (n=16)**	**P-value**
Number of Injection	**1**	**1**	
CMT (mean±SD)			
Baseline	592.06±158.78	552.69±197.049	0.538
6 weeks	354.31±81.62	359.94±98.53	0.826
Change of CMT (mm, mean±SD) (resolution of macular edema, %)			
1 month	237.75±95.82 (40.15±60.35)	192.75±117.66 (34.87±59.71)	0.624

Here, table: 3 show the elevations in IOP in both groups. The mean IOP in IVT and IVB groups at baseline was 16.650±2.87 and 16.56±2.421 respectively. After injection and 6 weeks follow-up we found an elevation in IOP in IVT and IVD groups (19.719±3.59 and 18.031±1.84 respectively). The mean elevation in IVT group was higher than IVB groups but the elevation was not statistically significant In concordance with this study by Nguyen et al found no elevation in IOP more than 15mm of Hg in IVT and IVB groups (10). Qamar et al also reported that IOP of the eyes treated with an IVT injection was significantly increased after one (17.7±1.1 mm/Hg; p<0.020), three (18.2±1.2 mm/Hg; p<0.003) and six months (18.1±1.320 mm/Hg; p<0.007) when compared to the baseline value (16.1±1.4 mm/Hg). The eyes treated with a PST injection displayed no significant increase in IOP after one (16.4±1.2 mm/Hg; p<0.450), three (16.3±1.1 mm/Hg; p<0.630) and six months (16.2±1.1 mm/Hg; p<0.720) when compared to the baseline value (16.2±1.3 mm/Hg) (9).

Table: 3 Comparison of IOP between IVT and IVB group

	IVT Group	**IVB Group**	**P-value**
Number of injection	1	1	
IOP (Mean±SD)			
Baseline	16.650±2.87	16.56±2.421	0.926
1st day	17.15±5.95	17.012±2.289	0.862
1st week	18.153±4.23	17.496±3.47	0.562
6 weeks	19.719±3.59	18.031±1.84	0.105

Moreover, our results showed that at 6 weeks after initial injections the reductions in ME was more remarkable in the IVT group than that in the IVB group (40.15% vs 34.87%), though there were again no statistical significance.

Ding et al (11) study also favor the our study that both IVT and IVB treatments can effectively improve BCVA and reduce CMT in patients with ME secondary to CRVO; no statistical difference were found in between the two treatment groups. However, triamcinolone acetonid cause more adverse effects than bevacizumab.

Overall, this study indicates that intravitreal injections of either IVT or IVB can both improve visual acuity and decreases ME in eyes with CRVO. The therapeutic effects of IVT showed more effective results as compared with IVB regarding anatomical and functional outcomes within 6 weeks after injection. However, the triamcinolone seemed to cause more adverse events than bevacizumad, including glaucoma and cataract progression.

This study although with small sample size, is randomized prospective study to compare the efficacy and safety of IVT and IVB in patients with ME associated with CRVO. It provided new and crucial evidence for the strategy for the treatment of ME associated with CRO.

Further larger multicentred clinical studies are needed to properly evaluate the efficacy and help to determine the optimal duration and interval between the injections.

IV. Conclusion

This study indicates that intraviteral injections of either TA or bevacizumab can both improve visual acuity and decrease ME in eyes with CRVO. But the therapeutic effects in between of IVT and IVB group was not much statistically significant regarding anatomical and functional outcomes within 6 weeks after injections.

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