

# COMPARISON OF VISUAL ACUITY AFTER FIRST INTRAVITREAL BEVACIZUMAB IN WET AGE RELATED MACULAR DEGENERATION AND CLINICAL SIGNIFICANT MACULAR EDEMA DUE TO OTHER CAUSES.

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## ABSTRACT

**PURPOSE:** To compare the visual acuity after the first intravitreal Bevacizumab (Avastin<sup>®</sup>) in wet age related macular degeneration and clinical significant macular edema due to other causes.

**METHODS:** An analytical cross sectional study was performed on consented patients with neovascular ARMD and clinical significant macular edema (CSME) due to other cause. All patients received 1.25 mg/0.05 ml intravitreal bevacizumab at baseline. Visual acuity at baseline was noted by using standard logMar chart. The patients were kept at follow up of 3 months. After 3 months, we checked the improvement of vision in both, Wet ARMD and CSME due to other causes.

**RESULTS:** 25 patients of ARMD and 25 patients of CSME received intravitreal bevacizumab for first time with the mean visual acuity of 1.0 log mar in both diseases. After the injection the maximum mean visual acuity improvement was 0.3 log mar in both of diseases with standard deviation of 0.94 in ARMD and 0.57 in CSME. The mean standard error was 0.18 in ARMD and 0.12 in CSME. Shapiro -Wilk distribution test showed non-parametric distribution in both groups (with  $p < 0.001$  in group). Therefore, Mann Whitney-U test was applied. This showed non-significant result in change in visual acuity between two groups. So, there is no significant difference in improvement of vision in both diseases after bevacizumab.

**CONCLUSION:** This study reveals that intravitreal Bevacizumab resulted in improvement of visual acuity in patients with wet age related macular degeneration and with CSME due to diabetes. There is no significant difference in visual improvement in both of diseases.

**KEYWORDS:** Visual Acuity, Macular degeneration, Macular Edema

## INTRODUCTION

Age related macular degeneration (AMD) is the degenerative disease that affects the macula and causes vision impairment which may results into the total visual loss. It is the leading cause of central vision loss in people over the age of 50 and affects the quality of life. The main risk factor for developing AMD is increasing age. It affects 30% of

individuals over the age of 70 and 60 million people worldwide.<sup>1</sup> Age related macular degeneration has two types: Dry AMD and Wet AMD. In dry AMD vision loss is associated with the drusenoid deposits in macula which results in photoreceptor degeneration, retinal pigment epithelium atrophy. On the basis of size and no of drusen AMD can be

divided into 3 stages early, intermediate and late AMD. Drusens are small yellow deposits in macula between the retinal pigment epithelium and the choroid. In early and intermediate AMD medium and large size drusens are present respectively but these two stages are usually asymptomatic. In late AMD along with the large drusenoid deposits there is symptomatic central visual loss. Dry AMD accounts for the 90% of AMD.<sup>1</sup> In wet AMD visual loss is because of the irregular veins development (choroid neovascularization). The multiplication of anomalous veins in retina are invigorated by vascular endothelial development factor (VEGF). The anomalous veins are delicate that prompts the blood and protein spillage underneath the macula. Bleeding, spilling and scarring from these veins influence irreversible harm to the photoreceptors and fast visual loss whenever left untreated. It is generally gone before by the dry AMD. Progression has been made in treatment of wet AMD with presentation of sheltered and powerful enemy of VEGF operators.<sup>2</sup>

Diabetic retinopathy is the intricacy of the diabetes and a main source of visual deficiency. It is the miniaturized scale angiopathy causing little veins harm due to high glucose.<sup>3</sup> Purpose behind loss of vision are Diabetic Maculopathy (DM) otherwise called clinically critical macular edema (CSME) and difficulties of proliferative diabetic retinopathy (PDR, for example, vitreous discharge, tractional retinal separation and neo vascular glaucoma. By 2030 the no of diabetic patients may ascend to 69% in creating nations. Diabetic macular edema is progressively regular in type 2 diabetes. A huge epidemiological investigation demonstrated that 26% of patients with diabetic retinopathy gave DME. As per another investigation, the commonness of macular edema in patients with as of late analyzed diabetes is 0 to 3%, expanding to 29% in diabetic patients with more than 20 years of infection. Clinical significant macular edema (CSME) is caused by disruption of inner blood retinal barrier, formed by the retinal vascular

endothelium due to hyper glycaemia, increased level of VEGF, inflammation and cytokines.<sup>4</sup> CSME may also involve the macula (center involving) or spare the central area (non center involving). Clinically critical macular edema (CSME) was characterized upon cut light bio microscopy as "(1) thickening of the retina at or inside 500  $\mu$ m of the focal point of the macula; or (2) hard exudate at or inside 500  $\mu$ m of the focal point of the macula related with thickening of neighboring retina; or (3) a zone of retinal thickening 1 circle territory or bigger, any piece of which is inside 1 plate width of the focal point of the macula.<sup>5</sup> The macular photocoagulation and against – VEGF specialists are powerful in diminishing visual loss from CSME.<sup>6,7</sup>

## MATERIALS AND METHODS

An analytical cross sectional, hospital based study conducted at Department of Ophthalmology, Mayo Hospital Lahore from September 2019 to December 2019. Fifty eyes of 52 patients received a single intravitreal injection of bevacizumab. The visual acuity was measured pre-injection and post-injection using standard log Mar visual acuity chart. Data was analyzed by Shapiro-Wilk test, Paired sample t test, Wilcoxon test and Mann Whitney-U test.

## RESULTS

25 patients of ARMD and 25 patients of CSME receive intravitreal bevacizumab for first time with the mean visual acuity of 1.0 log mar in both diseases. After the injection the maximum mean visual acuity improvement was 0.3 log mar in both of diseases with standard deviation of 0.94 in ARMD and 0.57 in CSME. The mean standard error was 0.18 in ARMD and 0.12 in CSME. (Table 1).

**Table - 1:**

Descriptive Statistics of Change in Visual Acuity in Two Groups								
Group	N	Minimum	Maximum	Mean		Std. Deviation	CI (95%)	
				Statistic	Std. Error		Lower Bound	Upper Bound
AMD	25	1	3	1.68	0.189033	0.945163125	1.56	2.07
CME	25	1	3	1.8	0.11547	0.577350269	1.56	2.04

Shapiro– Wilk distribution test showed non-parametric distribution in both groups (with  $p < 0.001$  in group). Therefore, Mann Whitney-U test was applied. This showed no significant result in change in visual acuity between two groups Fig. 1.

**Figure 1:** Statistical analysis between changes in visual acuity in two groups.

**Hypothesis Test Summary**

	Null Hypothesis	Test	Sig.	Decision
1	The distribution of Change in VASamples after injection is the same across categories of Group.	Independent-Samples Mann-Whitney U Test	.299	Retain the null hypothesis.

Asymptotic significances are displayed. The significance level is .05.

**DISCUSSION**

In this study, 50 eyes of 52 patients with 25 eyes having clinical significant macular edema and 25 eyes having age related macular degeneration were studied. In CSME, pre injection out of 25 eyes, 8 eyes have BCVA 1.0 log Mar, 6 eyes have 0.9 log Mar, 6 eyes have 0.8 log Mar and 5 eyes having 0.7 log Mar. In CSME the mean macular thickness was 470.76 microns with standard deviation of 17.47 +/- 3.49 prior to injection. In AMD out of 25 eyes pre injection BCVA was 1.3, 1.0 and 0.9 log Mar in 8,10,7 patients respectively. The mean macular thickness in ARMD was 295.24 microns with standard deviation of 19.67 +/- 3.93 prior to injection. Up to first month after the first intravitreal bevacizumab the patients shows a little improvement in visual acuity followed up by two months.

Three months after the injection in CSME, BCVA

improved up to 0.9, 0.8, 0.7, 0.6, and 0.5 log Mar in 6, 2, 4, 9 and 4 patients respectively. In CSME the mean macular thickness decrease by 30 % which was 440.36 microns with standard deviation of 17.06 +/- 3.41. In ARMD, BCVA post injection after 3 months was 1.0, 0.9, 0.8 and 0.7 log Mar in 8, 10, 6 and 1 patient respectively. The mean macular thickness in ARMD decreases by 20 % which was 274.32 microns with standard deviation of 18.71 +/- 3.74. There is significant change in vision before and after IV bevacizumab in CSME and in ARMD. Thus, in comparing the visual acuities after 3 months in CSME and in ARMD the p value is less than 0.05 in CSME and more than 0.05 in ARMD which means it is significant in CSME and in significant in ARMD.

Other infusion related unfavorable occasions, for example, endophthalmitis, vitreous discharge and retinal separation were not watched. Based on results visual sharpness improvement in CSME was greatly improved after intravitreal bevacizumab when contrasted with ARMD.<sup>8</sup> The abatement in mean macular thickness was seen to be more in CSME when contrasted with ARMD after the three months follow up of patients. Hence we improve consequences of bevacizumab in clinical noteworthy macular edema than age related macular degeneration.

Another investigation was acted in Denmark on the Optical intelligibility tomography and vessel measurement changes after intravitreal bevacizumab in diabetic macular edema. Intravitreal organization of bevacizumab was trailed by a mean increment in BCVA which was 7.3 +/- 17 letters. This was joined by a decrease in foveal subfield thickness from 447 +/- 117 micron meter to 334 micron meter.<sup>9</sup> Hallym University of Korea shows the same result on usage of bevacizumab for DME.<sup>6</sup> A comparative report was acted in Iraq on the treatment of bevacizumab for the diabetic macular edema by Dr. Salah Zuhair in 2011 in Thi-Qar University. In this investigation, patients follow up time was 3 months. The base

line vision was 0.73 +/-0.36 Log MAR, improved up to 0.63+/-0.41, 0.58+/-0.36, and 0.61+/- 0.40 Log MAR ( $p=0.006$ ) at multi week, 1 month, and at month 3.<sup>10</sup> Another investigation on the use of bevacizumab for Neo vascular AMD was distributed in July 1, 2005 which uncovers the improvement of macular appearance was kept up for at any rate a month, and vision stay stable. No aggravation was seen. Bevacizumab gives a viable, safe, and economical alternative for the people losing vision because of Wet AMD.<sup>11-13</sup> Transient security and adequacy of bevacizumab for Wet AMD, Eye institute of Florida shows that in 3 months visit, the normal number of infusions, 2.3 to limit of 4 infusions. No genuine medication related visual or foundational unfavorable occasions were distinguished. Upgrades in visual acuity and retinal thickness estimations were clear by week 1 and proceeded through month 3. In the month 3, the mean visual acuity improved from 20/160 to 20/125 and the mean RT diminished by 99.6  $\mu\text{m}$ .<sup>14</sup> Another study conducted by Jyothi in 2009 on bevacizumab for AMD shows same result.<sup>2</sup> All of the above studies show the effectiveness and long term efficacy and safety of intravitreal bevacizumab in clinical significant macular edema (CSME) and age related macular degeneration (ARMD). This study was conducted to check the ratio of improvement of vision in CSME and ARMD patients with the help of OCT reports of macular thickness before and after bevacizumab we notice the total reduction in CMT as well as comparison of CMT in ARMD and in CSME. All of the above studies shows similar results in vision improvement as this study did.

## CONCLUSION

This study revealed that intravitreal avastin resulted in improvement of visual acuity in patients with wet age related macular degeneration and with CSME due to diabetes. There is no significant difference in visual improvement in both of diseases.

## RECOMMENDATIONS

This study reveals that outcomes of intravitreal bevacizumab in CSME due to diabetes and in Wet ARMD patients were remarkable as it improves the visual acuity in short time period of 3 months intravitreal bevacizumab is also safe showing no adverse effect. The stability and more improvement in visual acuity can be observed by changing the time duration and frequency doses of intravitreal bevacizumab in long term.

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## REFERENCES

1. Chandramohan A, Stinnett SS, Petrowski JT, Schuman SG, Toth CA, Cousins SW, et al. Visual Function Measures in Early and Intermediate Age-Related Macular Degeneration. *Retina*.

- 2016;36(5):1021-31.
2. Jyothi S, Chowdhury H, Elagouz M, Sivaprasad S. Intravitreal bevacizumab (Avastin) for age-related macular degeneration: a critical analysis of literature. *Eye (Lond)*. 2010;24(5):816-24.
  3. Seo JW, Park IW. Intravitreal bevacizumab for treatment of diabetic macular edema. *Korean J Ophthalmol*. 2009;23(1):17-22.
  4. Wu L, Fernandez-Loaiza P, Sauma J, Hernandez-Bogantes E, Masis M. Classification of diabetic retinopathy and diabetic macular edema. *WJD*. 2013;4(6):290.
  5. Rotsos TG, Moschos MM. Cystoid macular edema. *Clin Ophthalmol*. 2008;2(4):919.
  6. Seo JW, Park IW. Intravitreal bevacizumab for treatment of diabetic macular edema. *Korean J Ophthalmol*. 2009;23(1):17-22.
  7. Wang Y-S, Xiao L, Wang H-Y, Zhang Z-F, Li M-H, Su X-N. Intravitreal bevacizumab combined with/without triamcinolone acetonide in single injection for treatment of diabetic macular edema. *Chin Med J*. 2011;124(3):352-8.
  8. Fang X, Sakaguchi H, Gomi F, Oshima Y, Sawa M, Tsujikawa M, et al. Efficacy and safety of one intravitreal injection of bevacizumab in diabetic macular oedema. *Acta Ophthalmol*. 2008;86(7):800-5.
  9. Soliman W, Vinten M, Sander B, Soliman KaEN, Yehya S, Rahman MSA, et al. Optical coherence tomography and vessel diameter changes after intravitreal bevacizumab in diabetic macular oedema. *Acta Ophthalmol*. 2008;86(4):365-71.
  10. Al-Asadi SZ. The Use Of Avastin (Becacizumab) For The Treatment Of Diabetic Macular Edema In Iraqi Patients. *Thi-Qar Medical Journal*. 2011;5(1):76-83.
  11. Rich RM, Rosenfeld PJ, Puliafito CA, Dubovy SR, Davis JL, Flynn Jr HW, et al. Short-term safety and efficacy of intravitreal bevacizumab (Avastin) for neovascular age-related macular degeneration. *Retina*. 2006;26(5):495-511.
  12. Rosenfeld PJ, Moshfeghi AA, Puliafito CA. Optical coherence tomography findings after an intravitreal injection of bevacizumab (Avastin®) for neovascular age-related macular degeneration. *Ophthalmic Surg Lasers Imaging*. 2005;36(4):331-5.
  13. Aggio FB, Farah ME, Silva WC, Melo GB. Intravitreal bevacizumab for exudative age-related macular degeneration after multiple treatments. *Graefes Arch Clin Exp Ophthalmol*. 2007;245(2):215-20.
  14. Brooks Jr H, Ashmore E, Barker D. Safety and efficacy of intravitreal Avastin for neovascular age related macular degeneration. *Invest Ophthalmol Vis Sci*. 2006;47(13):5212-.