

Original Research Article

Visual outcome versus vision satisfaction after intravitreal Bevasizumb injection in diabetic retinopathy.

Abstract:

Introduction:Diabetic retinopathy as an important complication of diabetes mellitus is a common cause of blindness in diabetic people. There is not available a curable treatment

this study is design to investigate the efficacy of the intravitreal injection of Avastin on visual and patient's satisfaction with diabetic retinopathy.

Material and Methods: This study included 30 eyes of 30 patients (mean age: 60.47 ± 8.94 years) with diabetic retinopathy showing no recovery with common treatments. After the intravitreal injection of 1.25mg/0.05ml of Avastin at the day of injection, the

examination was performed. In these examination, the resolution of neovascularization , clearance of vitreous and visual acuity versus vision satisfaction were evaluated.

Results: 60% of patients were women (n=18) and 40% were men (n=12). All patients had type 2 diabetes for a period of 8.47 ± 5.28 years (range 2-25 years). Change in best corrected visual acuity (BCVA) in right eye was 0.22 ± 0.63 log MAR which it was statistically significant ($p=0.010$). The BCVA in left eye was 0.31 ± 0.74 log mar that it showed also significant relation ($p=0.020$). BCVA Changes had not a meaningful relationship with age and sex of patients, but had a negative meaningful relationship with duration of diabetes retinopathy in both right and left eyes. ($p=0/048$, $p=0/006$ respectively).

Conclusion: Avastin showed long time clinically significant visual benefit but it was not compatible to the patient visual satisfaction. So, the future studies will be needed to determine the therapeutic effect of this treatment option.

Key words: diabetic retinopathy, vision satisfaction, Avastin.

Introduction:

The early treatment diabetic retinopathy study (ETDRS) demonstrated that immediate focal photocoagulation reduced moderate visual loss by 50, this suggests that a distinct subgroup of eyes exists with diabetic macular edema (DME) resistant to conventional laser photocoagulation.¹

Vitrectomy or application of focal macular laser and panretinal photocoagulation at appropriate disease stages reduces the risk of further vision loss. While triamcinolone 3-year visual benefit was found to be inferior to standard focal macular laser, Ongoing research will determine the utility of inhibitors of vascular endothelial growth factor as an additional tool in the management of diabetic retinopathy.^{1,2}

The M. Michaelides et-al finding support the use of bevacizumab in patients with persistent nonischemic center-involving (clinically significant macular edema)CSME but they was not able to find the benefit despite the relatively long duration of CSME and high number of previous laser treatments at baseline.³

There are others studies that indicate intravitreal bevacizumab for DME which have severe capillary loss showed beneficial effects on vision and favorable remodeling of the macular architecture. They conclude no major adverse event related to treatment during the 54-week follow-up.⁴

As described by R. L. Avery and colleagues it remains unclear how frequently repeat anti-VEGF therapy would be necessary to ensure regression of neovascularization, and panretinal photocoagulation clearly seems to be a preferred treatment for chronic intravitreal injections.⁵

The overwhelming evidence for intravitreal bevacizumab's role in the treatment of retinal disease was our encouragement to done this study which explained our experience with this emerging of treatment.

Material and Methods

The 30 eyes of 30 patients who had CSME or proliferative diabetic retinopathy enrolled in this study. The worth eye or the only one eye underwent of intravitreal injection of bevacizumab. Exclusion criteria were intravitreal steroids within the last 4 months, of intraocular injection of anti-VEGF within the last 3 months, macular ischemia more than one disc diameter, and priors' history of intraocular surgery within at last 6 months ago. Patients with thromboembolic events or uncontrolled hypertension also excluded of study. Informed consent was obtained from all patients.

A complete ophthalmic examination at baseline and thereafter by every visit during the follow-up, including BCVA using standard Snellen charts, ophthalmoscopy and fluorescein angiography (Topcon, Topcon Corporation, Tokyo, Japan) was done. All the patients completed a follow-up time of at least 3-36 months and filled a satisfaction shield composed of 1- improved vision 2- No improved vision 3-not noticeable or worsted.

Under topical anesthesia a lid speculum inserted and the povidone-iodine 5% was applied to conjunctival sac and lid margins. The 1.25 mg bevacizumab injections were undertaken with a 27-gauge needle through the supra- temporal quadrant. The patients taken one to three injections and were followed monthly. Reinjection was performed if retinal thickening remained clinically and no improvement observed in visual acuity indeed of fluorescein leakage which involving the center of the macula.

All visual acuities were converted to logMAR before analysis for statistical purposes. Due to the small number of patients, the Wilcoxon matched pairs test was used for the statistical analysis of the data. A *p*-value less than 0.05 were considered to be the threshold for significance.

The outcome measurement was comparison of the mean ETDRS BCVA at 3-36 months follow up between pre and post IVB injection. The others variable was relating to safety in ocular side effects and systemic side effects according to patients complain. The third was assessment of visual satisfaction of their visual outcome.

Results

Of 30 patients who enrolled in the study, 40% (No=12) was men and 60 % (No= 18) were female the mean ages was $94 / 8 \pm 47/60$ years ranged from 39 to 83 years. (Table 1)

Visual acuity showed improvement but the patients have not satisfaction according to before and after bevacizumb interavitreal injection in their eyes. As it showed in figure 1 and table 2 and ,3 this improvement difference have not a brisk insult and it was with this effect of the patient unhappiness. The new vessels regressed vigorously after interavitreal injection but after one month again appeared (figure 2,3). Complication in

this study was retinal detachment after second injection in one patient, two cases also developed the temporary mild anterior uveitis without pain or others eye complain such as vitritis, hypopyon, and blurred vision. The inflammation resolves in few days by topical steroid treatment.

Discussion:

There was clinically significant difference in visual improvement at right and left eye before and after injection, but the patient's does not have visual outcome satisfaction in spit of this significant difference in objective test evaluation. The studies by M.J Elman and Fernando Arevalo .J with colugos about ranibizumab or focal/grid laser, or both they indicate that additional studies are needed to can judge the success criteria which met early in the course of treatment.^{6,7}

So, the other researcher as described in the below are not sure about this therapeutic option,^{8,9, 10} They suggests that intravitreal bevacizumab is not an effective treatment for diffuse DME, in contrast to other reports. An explanation for this different finding was thought to be the criteria they used to define diffuse DME.¹¹

R. Simo and C. Hernandez also belived that Bevacizumab is a off-label medicine that many ophthalmologists used it because it is as effective as pegaptanib or ranibizumab but is much cheaper. In this regard, they conclude more clinical trials designed to evaluate not only efficacy, but also systemic adverse effects of anti-VEGF therapy .⁹

Our study showed statistically significant difference in VA outcome after intravitreal bevasizumb injection either due to diabetes maculopathy or proliferative retinopathy, the most excellent response was in the first month post injection. After 3 months of ranibizumb we could not find stable diabetic maculopathy or proliferative diabetic retinopathy either by permanently preventing of retinal and iris neovascularisation or macular edema which gradually appeared again. So our finding were agree with Matsuda S et al in one direction of their study that it does not show any significant difference related to number of intravitreal injection in the $HbA1c \leq 7.0\%$ group compared to $HbA1c > 7.0\%$ group. They also suggested that glucose regulation can impact the response to anti-VEGF therapy in the management of DME¹².

Few patient developed mild anterior chamber reaction with full recovery by topical steroid. Except of one case which have two injection due to macular edema and denied operation which lost the left eye after rhegmatogenous and tractional retinal detachment. The questionnaire satisfaction was prepared to find how much patient agreement is in their visual improvement that it was not compatible to visual finding outcome. The Ferenchak K and colugos study described twelve eyes of nine patients of intravitreal bevacizumab (IVB) for eyes with recurrent vitreous hemorrhage after vitrectomy for proliferative diabetic retinopathy. They conclude that in their study none of twelve eye required repeat vitrectomy for recurrent VH. Mean follow-up was 22 months (range, 8-42). A mean of 8.1 IVB (range, 1-18) were given Intravitreal bevacizumab was a safe and effective adjunct in this series for the management of recurrent VH after vitrectomy for proliferative diabetic retinopathy.¹³ In a review study by. Nicholson B. P and. Schachat A. P they described in spite of short-term benefit in visual acuity, but this treatment may be associated with tractional retinal detachment. Finally they concluded despite promising early reports on the safety of these medications, we will be await to knows more results of the safety and efficacy of anti-VEGF drugs for diabetic retinopathy.¹⁰ Our study also showed the same suggestion as above described by Nicholson B.P and Schachat A.P but one case develop retinal detachment.

The Spearman correlation coefficient between age and visual changes before and after injection in the right and left eye dose not demonstrate any significant relationship. ($p = 0.222$, $p = 0.913$). But the Spearman correlation coefficient showed that duration of diabetes has a negative relationship in both eye visions before and after injection. ($p = 0.048$, $p = 0.006$) This means that the longer duration of diabetes reduced the vision improvement change before and after of injection in both eye.

Limitations of our study are nonrandomized, uncontrolled, and retrospective, which preclude any estimation of efficacy or safety of intravitreal bevacizumab. In addition, due to no control group we cannot rule out the possibility of improvement in macular edema might be associated with systemic health attention. However, the results were very promising but it suggest the need for further investigation.

In summary, although it taken many years of intravitreal bevacizumab injection and the preliminarily reports which claimed stability and improvement in VA, the future over all argumentative reports will be make any specific treatment recommendations. So, in spit of many promising results but it is too soon to judgment the safety and efficacy and cost effectiveness of this treatment.

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Table 1. Maximum, minimum, mean and median variables under study in the studied patients

Variable	No	Min	Max	Mean $\pm$ Sd	median
Age	30	30	83	60.47 $\pm$ 8.94	59.5
Duration of right eye F/U	17	3	32	11.94 $\pm$ 9.04	9
Duration of left eye F/U	26	3	36	14.23 $\pm$ 9.84	12
Number of injection on R E	17	1	3	1.24 $\pm$ 0.56	1
Number of injection on L E	26	1	2	1.23 $\pm$ 0.43	1
Diabetes duration	30	2	25	8.47 $\pm$ 5.28	7

F/U = Follow-up, LE = Left eye, R E = Right eye

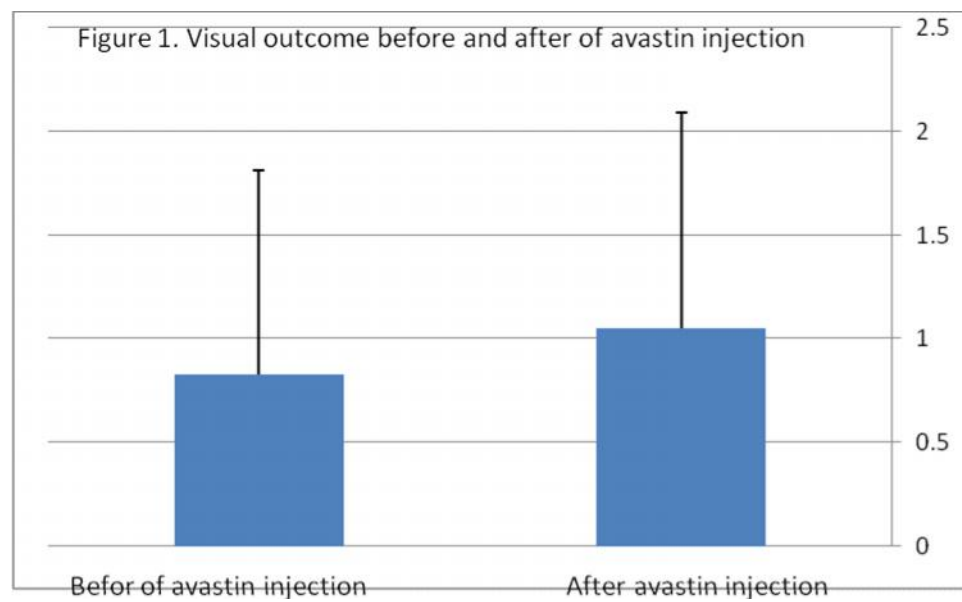


Table 2. Comparative study of visual acuity difference before and after intravitreal avastin injection according to diabetes duration and age.

	Diabetes duration		Age	
	Spirman	P-Value	Spirman	P-Value
Difference of VA of R eye (according to LOG-MAR)	-0.364	-0.048	0.230	0.222
Difference of VA of L eye (according to LOG-MAR)	-0.490	-0.006	0.021	0.913
VA= visual acuity, L = Left, R = Right, LOG-MAR = Logarithm of minimum angel resolution.				

Table. 3 Comparative study of visual acuity difference before and after intravitreal avastin injection according to right and left eye.

	Before avastin injection (according to LOG-MAR)	After avastin injection (according to LOG-MAR)	
	Mean $\pm$ SD	Mean $\pm$ SD	P-Value
VA of R eye	1.05 $\pm$ 1.04	0.83 $\pm$ 0.98	0.01
VA of L eye	1.34 $\pm$ 0.85	1.03 $\pm$ 0.80	0.02
VA= visual acuity, L = Left, R = Right, LOG-MAR = Logarythm of minimum angel resolution.			

Figure legends:

Figure 2. A&B: Right and Left iris neovascularisation Date; 7/06/2009 .

, Date; 14/4/2010 C&D:Right and Left iris neovascularisation

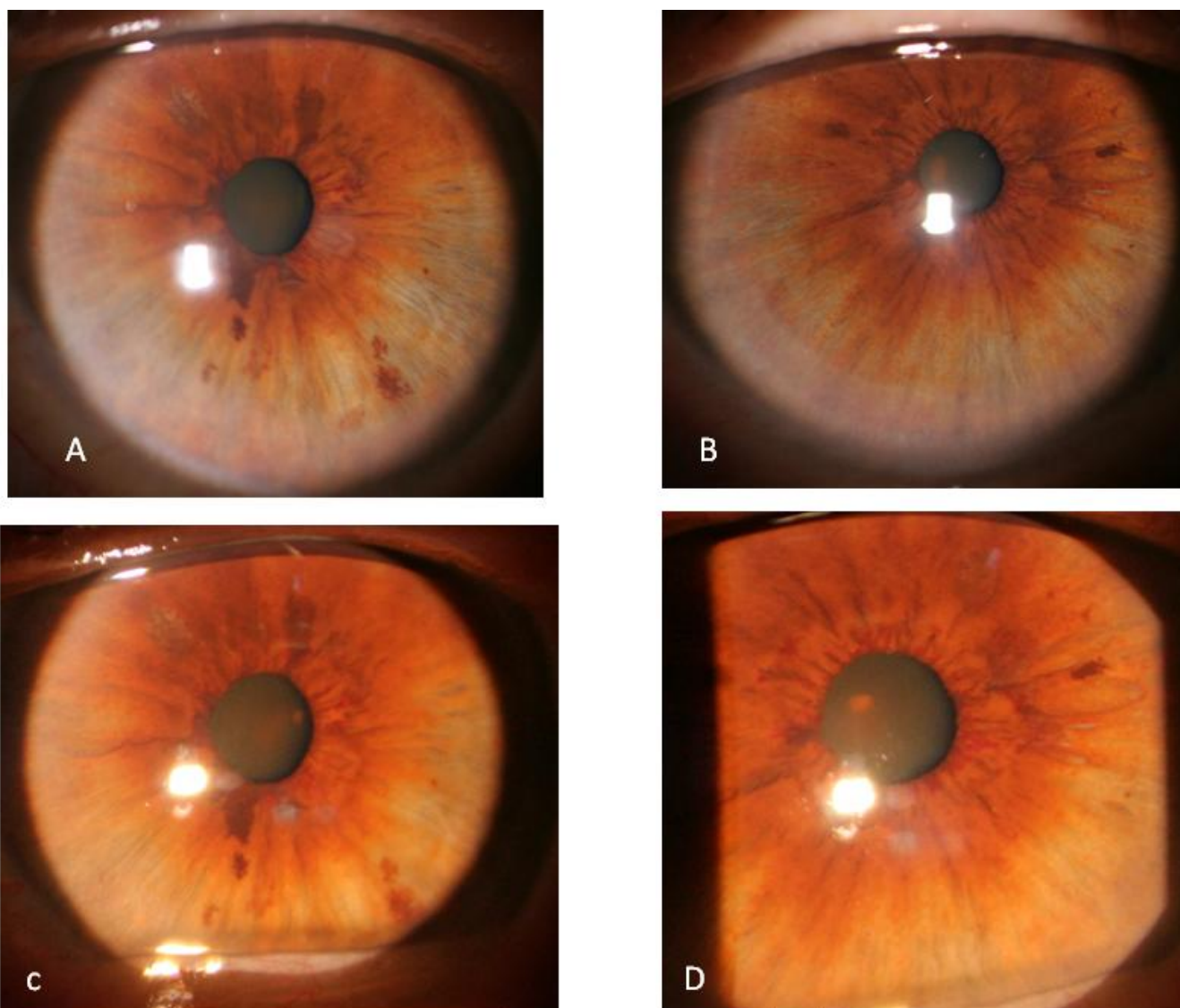


Figure 2. A&B: Right and Left iris neovascularisation Date; 7/06/2009 .
C&D:Right and Left iris neovascularisation , Date; 14/4/2010

Figure 3.A&B: Disappearance of Right iris neovascularisation Date; 0/6/2010, C Disappearance of Right iris neovascularisation and D reappearance of Left iris neovascularisation Date; 18/6/2011

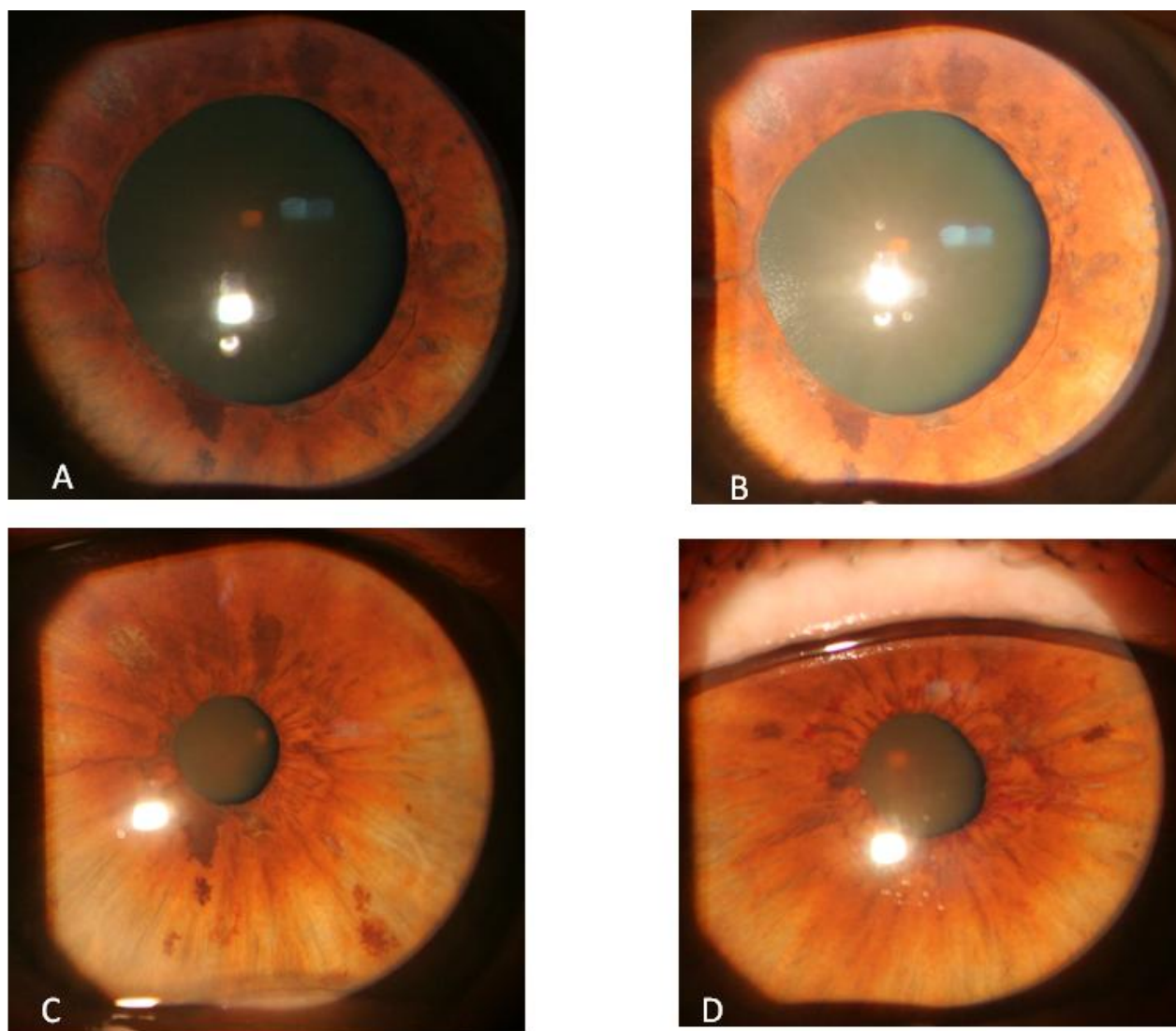


Figure 3.A&B: Disappearance of Right iris neovascularisation Date; 0/6/2010, C Disappearance of Right iris neovascularisation and D reappearance of Left iris neovascularisation Date; 18/6/2011