

Intravitreal Avastin as a Treatment of Diffuse Diabetic Macular Edema

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Abstract

Background: Macular edema, defined as retinal thickening within 2 disc diameters of the center of the macula, results from retinal microvascular changes that compromise the blood-retinal barrier, causing leakage of plasma constituents into the surrounding retina and, consequently, retinal edema. Focal edema is associated with hard exudate rings caused by leakage from micro aneurysms. Diffuse edema is caused by leakage from micro aneurysms, retinal capillaries, and arterioles.

Avastin (Bevacizumab) is a recombinant humanized monoclonal IgG1 antibody that binds to and inhibits the biologic activity of human vascular endothelial growth factor (VEGF). It contains human framework regions and the complementarity-determining regions of a murine antibody that binds to VEGF. Avastin produced in a Chinese Hamster Ovary mammalian cell expression system in a nutrient medium containing the antibiotic gentamicin and has a molecular weight of approximately 149 kilo Daltons.

Purpose: To assess the anatomic effect and visual acuity response after intravitreal (Avastin) in patients with diffuse diabetic macular edema.

Patients and Methods: This study included 15 eyes of 15 Patients with stable diabetes mellitus with diffuse diabetic macular edema. All eyes had received some form of argon laser photocoagulation (pan retinal photocoagulation (PRP), Focal or Grid of duration not less than 6 months. Mean age of 59 years treated with two intravitreal injections of Avastin 1.25 mg in 0.05 ml six weeks apart. Patients were examined by experienced ophthalmologist visual acuity, evaluation of diabetic retinopathy, central macular thickness by optical coherence tomography each was evaluated at the beginning of study (baseline) and follow-up visits.

Results: 15 eyes of 15 diabetic patients with persistent diffuse macular edema with no improvement in visual acuity. All the patients received two injections of Avastin six weeks apart. No complications were observed in any patient. The mean baseline visual acuity was (log Mar=1.338±0.455) and the mean visual acuity at three months following the second intravitreal injection was (log Mar=1.094±0.254), the mean central macular thickness at baseline was 492 µm decreased to 369 µm at the end of three months.

Conclusions: Avastin resulted in a significant decrease in macular thickness and improvement in visual acuity at three months after the second injection.

Keywords: Diffuse diabetic macular edema, intravitreal Avastin, vascular endothelial growth factor, central macular thickness

Patients and Methods

Prospective study included 15 eyes of 15 patients (8 females and 7 males) with diffuse diabetic macular edema assessed by fluorescein angiography (FFA), best corrected visual acuity ≤ 0.133 , HbA1C $\leq 7.0\%$. Patients with uncontrolled diabetes, hypertension or chronic renal failure. Patients subjected recently to laser therapy, patients

with other macular pathology or optic disc pathology were excluded.

All Patients subjected to ophthalmic assessment including best-corrected visual acuity, Bio microscopic anterior segment examination, fundus examination with +90D lens and Fluorescein angiograph. Central macular thickness was measured with optical coherence tomography (OCT). The study parameters were evaluated one month and three months after the second intravitreal Avastin injection.

Technique:

- Instillation of local anesthetic drops.
- Avastin is drawn up under sterile condition.
- Disinfection of the eye using 5% aqueous povidone iodine solution.
- Lid speculum is used to hold the eye open.
- Swab soaked in local anesthetic placed over the site of the injection and hold for 60 seconds.
- Measuring caliper used to measure a safe distance behind the limbus.
- 1.25mg / 0.05cc Avastin injected with 30G needle in infratemporal quadrant.
- Instillation of topical antibiotic.
- Patient's vision is checked for any sudden visual defect.
- Topical antibiotic drops for 7 days after the injection as prophylaxis.

Six weeks after first injection, second injection was given in similar circumstances. Visual acuity, central macular thickness and side effects, local or systemic complications were evaluated.

Results

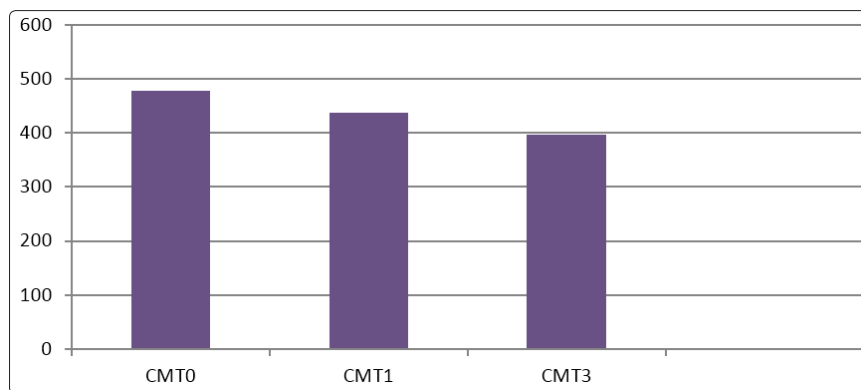
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Table 1: Outcomes in 1month and 3 months after the second Avastin injection:

Age of Patients	Gender of Patients	Previous laser	BCVA-Base line	BCVA-1 month	BCVA-1 month	CMT-Base line microns	CMT-1 month microns	CMT-3 month microns
672	705	790	0.10	0.1	0.05	Grid	M	59
587	620	810	0.20	0.17	0.10	Focal	M	45
335	340	360	0.10	0.1	0.05	PRP+ Focal	F	55
356	370	392	0.133	0.133	0.10	PRP	F	60
313	368	383	0.33	0.25	0.133	Focal	F	63
280	295	306	0.10	0.10	0.05	PRP	M	62
410	446	460	0.20	0.20	0.17	PRP+ Focal	F	65
502	528	575	0.10	0.10	0.05	Grid	M	60
492	571	598	0.20	0.17	0.17	PRP+ Focal	F	59
289	380	370	0.33	0.25	0.133	Focal	M	58
367	372	410	0.17	0.10	0.05	Grid	F	52
325	375	423	0.20	0.133	0.10	Focal	F	64
356	435	395	0.17	0.17	0.133	PRP+ Focal	F	60
320	391	462	0.25	0.20	0.17	Focal	M	54
348	378	428	0.25	0.25	0.17	PRP+ Focal	M	56

Outcomes in 1month and 3 Months after the Second Avastin Injection

At month 3 after the second injection, the mean central macular thickness was 369.8 µm. During the entire follow-up of 3 months, there were no cases of clinically evident local or systemic complication such as endophthalmitis, increased IOP, retinal detachment, cerebrovascular accidents, transient ischemic attacks, myocardial infarctions or peripheral vascular disease.



CMT 0 - Mean baseline central macular thickness
CMT 1 - Mean central macular thickness at 1 month
CMT 3 - Mean central macular thickness at 3 months

Figure 1: Changes in the Mean Central Macular Thickness through Study Interval

Discussion

Diabetic macular edema (DME) is important cause of visual loss in diabetic patients and often leads to legal blindness if not treated. Argon laser photocoagulation and intravitreal triamcinolone acetonide are the common treatment options used for the various forms of DME. United Kingdom Prospective Diabetes Study reported that most eyes with diffuse diabetic macular edema which treated with laser photocoagulation do not have an improvement in VA [1-12].

Avastin has been considered as another treatment option in DME after the establishment of the role of vascular endothelial growth factor (VEGF) in the enhancement of retinal neovascularization and increasing vascular permeability in diabetic Patients. In this study intravitreal Avastin injection given to 15 eyes with diffuse diabetic macular edema resulted in both anatomic and functional improvement in form of reduction in central macular thickness and improvement of best-corrected visual acuity. The results also show that Avastin was well tolerated and no local or systemic complication were reported during the study.

Conclusions

Avastin resulted in meaningful reduction of central macular thickness and improvement in visual acuity at three months interval after second injection. The use of avastin to inhibit vascular endothelial growth factor (VEGF) associated with neovascularization and increased retinal vascular permeability in diabetic retinopathy produce significant improvement in case of diffuse diabetic macular edema.

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