

Anti-VEGF Monotherapy for Neovascular Age-Related Macular Degeneration in Vitrectomized Eyes



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Introduction

Neovascular age-related macular degeneration (N-AMD) is the most common cause of legal blindness in the western world.¹ Intravitreal anti-VEGF agents, bevacizumab (Avastin) and ranibizumab (Lucentis) are currently the most effective treatment for N-AMD.²⁻⁴ Patients are treated with monthly injections, at least initially, although less frequent injections may be appropriate after three to four loading injections in some patients. Both bevacizumab and ranibizumab appear to have equal efficacy.⁴

In the rabbit eye, vitreous half-life of intravitreal 0.5 mg ranibizumab was 2.88 days, shorter than 4.32 days for the half-life of 1.25 mg intravitreal bevacizumab. Both drugs were detectable in the vitreous at one month.⁵⁻⁶ Pharmacokinetics of these agents has not been studied in vitrectomized eyes.

Intravitreal bevacizumab was ineffective in the management of diabetic macular edema in eyes that had undergone a vitrectomy procedure, presumably due to rapid clearance of the drug in such eyes.⁷ However, this information may or may not be applicable to the eyes with N-AMD. No information exists regarding the efficacy of these agents as monotherapy in the management of N-AMD in vitrectomized eyes.

Methods

We performed a retrospective chart review of 9 eyes with N-AMD that had undergone previous pars plana vitrectomy and were treated with anti-VEGF monotherapy. Eyes were divided into two groups:

Treatment Naïve (Four Eyes): These eyes underwent a vitrectomy procedure for a macular hole, macular pucker, retinal detachment and acute postoperative endophthalmitis 7, 22, 48 and 22 months prior to the onset of N-AMD. Diagnosis of N-AMD was established by recent onset of symptoms, clinical examination, spectral domain OCT and intravenous fluorescein angiography. Baseline lesion characteristics and central field OCT thickness were recorded. All eyes were initially treated with monthly intravitreal anti-VEGF injections, 1.25 mg bevacizumab (Avastin) in 0.05 mL in three eyes, and 0.5 mg ranibizumab (Lucentis) in one. Therapy was guided primarily by VA, clinical examination and spectral domain OCT findings.

Monthly injections were continued until the lesion was completely dry and only then interval between injections was gradually increased. Rescue therapy with intravitreal triamcinolone or half-fluence PDT combined with anti-VEGF injection was considered for lesions that showed persistent activity despite monthly anti-VEGF injections.

Eyes With Prior AMD (Five Eyes): These eyes were being treated with anti-VEGF monotherapy at the time of PPV, which was performed 3-47 months (mean 15) after the diagnosis of N-AMD for vitreo-macular traction (2 eyes), acute postoperative endophthalmitis following cataract surgery (2 eyes) and macular hole (1 eye). Evaluation and treatment plan was the same as described for treatment naïve eyes. Eyes with at least 6 months follow-up were included for further analysis. Visual acuity, OCT findings and findings from clinical examination or fundus photos were recorded at the time of final follow-up visit. Change of ≥ 0.2 logMAR units was considered significant.

Results

Treatment naïve group: (Table 1) Mean age of patients was 77.7 (range 69-83) years (M=1, F=3). Baseline Snellen VA at the time of diagnosis of N-AMD was 20/25, 20/70, 20/400 and 20/25 respectively, mean 20/63. Baseline OCT thickness was 346.5 microns (range 220-491). All eyes had a PCIOL. Three had occult CNVM and 1 classic. Lesion size was one disk area in all eyes. Treatment consisted of monthly intravitreal injections of Avastin (3 eyes) and Lucentis (one eye). After 15, 25, 21 and 6 (mean 17) months follow up, all eyes showed improved (2 eyes) or stable (2 eyes) vision (Mean 20/46, range 20/20-20/200). A total of 14, 21, 16, and 5 anti-VEGF injections (Mean 14.75) were given respectively. Case 1 was switched to Lucentis after 9 Avastin injections due to persistent neovascular activity. Case 3 also required 3 intravitreal triamcinolone injections (4 mg/0.1 mL) and a PDT, and developed subretinal fibrosis.

Table 1: Treatment Naïve Group

Case	Age Sex	Reason for PPV	Time between PPV and N-AMD (mos)	Baseline VA at PPV	Baseline OCT	Lesion Type and size	Therapy	Final VA	Final OCT	Follow up (months)
1	69F	MH	7	20/25	220	Occult 1DA	Av9Lu5	20/30	206	15
2	83F	ERM	22	20/70	337	Occult 1DA	Av21	20/40	244	25
3	78M	RD	48	20/400	491	Classic 1DA	Av10Lu6 IVK3PDT	20/200	268	21
4	81F	Endophthalmitis	22	20/25	338	Occult 1DA	Lu5	20/20	274	6

Eyes With Pre-existing N-AMD: (Table 2) Mean Age of patients was 78.4 years (range 69-95, M=2, F=3). N-AMD was diagnosed a mean of 14.8 months (range 3-47) months prior to PPV, which was performed for a full thickness macular hole (one eye), vitreo-macular traction (2 eyes) and endophthalmitis following cataract surgery (2 eyes). Prior to PPV, all eyes were treated with anti-VEGF injections (Mean 8.6, range 2-25, all except one injection consisted of Avastin). All eyes had occult lesions, measuring one disk area. Baseline VA after PPV was 20/172 (range 20/60-20/400). After PPV, intravitreal Avastin was continued in three eyes, and two eyes were treated with intravitreal Lucentis. Patients were followed up for a mean of 16.6 months (range 7-34), and received a mean of 13.4 (range 7-24) injections. One eye was switched from Avastin to Lucentis after nine injections, and was treated with PDT after 5 Lucentis injections. Mean final VA was 20/178 (range CF-20/30), improved in three eyes, remained stable in one and declined in one eye. Decrease in vision in that eye was attributed to central geographic atrophy. None of the eyes developed subretinal fibrosis. Mean OCT thickness at final follow-up was 244 microns (range 162-327).

Table 2: Eyes With Pre-existing N-AMD

Case	Age Sex	Reason for PPV	Time between N-AMD and PPV (mos)	Baseline VA after PPV	Baseline OCT after PPV	Lesion Type and size	Therapy	Final VA	Final OCT	Follow up (months)
1	95M	VMTS	3	20/400	142	Occult 1DA	Av11	20/200	162	12
2	86F	Endophthalmitis	4	20/200	303	Occult 1DA	Lu7	20/200	200	7
3	69F	MH	3	20/80	269	Occult 1DA	Av9Lu5 PDT	CF	268	18
4	73F	VMTS	17	20/400	368	Occult 1DA	Av8Lu1 6	20/200	290	34
5	69M	Endophthalmitis	47	20/60	403	Occult 1DA	Av5Lu6	20/30	327	12

Discussion

Half the eyes in treatment naïve group responded well to the initial anti-VEGF monotherapy. One eye responded well to switch to ranibizumab after 9 bevacizumab injections. One eye required rescue therapy with intravitreal triamcinolone and PDT. In general, patients in this group presented with small lesion and good baseline VA, which might favorably influence the outcome.⁸

Eyes with pre-existing N-AMD also did well anatomically with anti-VEGF monotherapy. The same anti-VEGF agent that was being given prior to PPV was continued after PPV in 4 eyes. Patients in this group had worse visual acuity, mostly due to pre-existing geographic atrophy. Only one eye required PDT, which was done in Case 3 to eliminate the need for injections in an eye with poor visual potential due to central geographic atrophy.

It is well established that the half-life of an intravitreal drug is reduced to half to one third in vitrectomized eyes. Therefore, one would have expected worse outcome in our patients. There are several explanations for reasonably good response in these eyes. First, lesions were relatively small, and patients had good baseline presenting visual acuity. Both these factors are associated with an improved visual outcome in N-AMD.⁸ Second, although drug may leave the vitreous cavity sooner after PPV, enough drug might remain bound at the target site to accomplish the therapeutic effect. Third, vitreous VEGF levels in N-AMD are relatively low. Therefore, a smaller amount of drug may be effective compared to a situation such as DME, where anti-VEGF levels are relatively high.⁹ Fourth, PPV was performed for VMTS in two of five eyes in Eyes With Pre-existing AMD group. Recent evidence suggests that vitreo-foveal adhesion and VMTS may play a role in the pathogenesis of N-AMD, and vitrectomy alone might cause regression of a choroidal neovascular membrane.¹⁰

Our study demonstrates that anti-VEGF monotherapy may provide encouraging results in patients with N-AMD who have undergone a prior vitrectomy.

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Financial Disclosures: None
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