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Efficacy of Intra Vitreal Injection of Anti VEGF Bevacizumab in the Treatment of Choroidal Neovascularisation

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Abstract: ***Aim: To evaluate the efficacy of intravitreal bevacizumab for the treatment of neovascular age related macular degeneration and to assess the improvement in visual acuity, reduction in macular thickness in optical coherence topography. Materials and Methods: A prospective non-randomized clinical study was carried out in 31 eyes in which 31 patients having CNVM were tested for visual acuity and macular thickness were checked before and after intravitreal injection of anti VEGF bevacizumab. Results: There were 2-line improvements in visual acuity by Snellen chart in CNVM patients. 95.65 % of classic CNV and 100% of occult CNV showed reduction in macular thickness. 1 case of Classic CNV showed no improvement till the end of the study because of macular scarring. Conclusion: Intravitreal bevacizumab (1.25 mg) treatment was well tolerated over 4 months with significant safety and efficacy.***

Keywords: Bevacizumab, Choroidal neovascularisation, Age-related macular degeneration, VEGF.

1. Introduction

In the developed world, one of the main causes of legal blindness is age-related macular degeneration (AMD).[1] Despite being less prevalent than atrophic AMD, neovascular AMD accounts for the majority of cases of significant vision loss linked to the condition [1–3]. Because it stimulates the proliferation of endothelial cells and raises vascular permeability, vascular endothelial growth factor (VEGF) has been connected to choroidal neovascularization (CNV) in AMD [4].

Photodynamic therapy (PDT) with verteporfin and argon laser photocoagulation are common treatments for CNV. The Macular Photocoagulation Study showed that argon laser photocoagulation might be used to cure well-defined or "classic" subfoveal CNV.[6–9] However, a central scotoma is frequently the result of irreversible photoreceptor loss from this procedure. PDT successfully decreased the probability of moderate to severe visual loss in situations of primarily classic subfoveal CNV, according to later major multicenter investigations.[10–12] Patients may still lose their eyesight before stabilization, even though PDT is intended to reduce retinal and retinal vascular damage.

Pegaptanib, a 28-base anti-VEGF aptamer, was licensed by the US FDA in December 2004 for the treatment of CNV. In the first year, pegaptanib-treated eyes outperformed controls, despite continuing to lose eyesight.[13, 14] Ranibizumab, a chemically modified and affinity-matured form of bevacizumab, is another anti-VEGF drug. The FDA has approved bevacizumab, a humanized monoclonal antibody that blocks all VEGF isoforms, to treat colorectal cancer [15]. Bevacizumab has recently been utilized to treat AMD-related CNV. Later, Rosenfeld and associates presented a case report of a single eye that had improved CRT and visual acuity four weeks after an intravitreal injection of 1.25 mg of bevacizumab. [16]

2. Materials and Methods

This was a Interventional, Prospective, Non-randomized clinical study done in Regional Institute of Ophthalmology, Rajendra Institute of Medical Sciences, Ranchi between March 2023 to January 2024. This study was conducted in accordance with the tenets of the declaration of Helsinki.

The study comprised patients with age-related macular degeneration (AMD)-related choroidal neovascularization (CNV), as determined by fundus fluorescein angiography (FFA) and optical coherence tomography (OCT), and with a best-corrected visual acuity (BCVA) of less than 6/24. However, individuals having a history of recent myocardial infarction, recent cerebrovascular accident, uncontrolled hypertension, vitrectomy, or uveitis were not included.

Following an explanation of the process, all patients provided written informed consent. Every patient had a brief history obtained before a comprehensive systemic and ophthalmic evaluation. A slit-lamp biomicroscope was used to investigate the anterior segment, while a 90D lens and a binocular indirect ophthalmoscope were used to evaluate the posterior pole. Detailed fundus drawings were also included. Photographs of the fundus were also taken for documentation. Additionally, fundus fluorescein angiography and optical coherence tomography were performed on each patient.

An intravitreal injection of 1.25 mg Bevacizumab (Avastin) in 0.05 ml was given to each subject. Following proper aseptic and antiseptic procedures, the injections were given in an operating room while under 0.5% proparacaine anesthesia. Using a 30-gauge needle, the injection was administered directly into the vitreous cavity via the pars plana route,

roughly 3.5 to 4 mm posterior to the limbus in the temporal quadrant.

To prevent an abrupt inflow via the vitreous cavity, the drug was administered gradually and steadily. Moxifloxacin eye drops were administered, followed by a pad and bandage for four hours. In order to lower the risk of elevated intraocular pressure (IOP), patients were additionally prescribed oral acetazolamide (250 mg) to be taken twice daily for two days. They were told to keep using Moxifloxacin eye drops four times a day for three days and to take off the pad and bandage after four hours.

Injections were given to patients every month till the neovascularization went away. The Snellen chart was used to test best-corrected visual acuity (BCVA), and SPECTRAL OCT was used to determine macular thickness. Regular follow-ups were planned for the patients at two, four, eight, twelve, and sixteen weeks. At every visit, fundus photos and OCT scans were recorded, and intraocular pressure and BCVA were measured.

Statistical Analysis

All the data were noted on MS Excel sheet and analysed using SPSS 21.0 package (SPSS Inc., Chicago, USA). Results of the analysis were evaluated under 95% confidence interval and mean values as mean± SD. The p value <0.05 was considered statistically significant.

3. Results

In our study, total number of patients were 31 in which male patients were 21 (67.74%) and females 10(32.25%) ; male: female 2.1: 1.Most of the patients were in the age group of 50-60 yrs 16(51.61%). Before giving injection, number of patients with visual acuity between hand movements to 1/60 were 12 (38.70%), between 2/60 to 4/60 were 15 (48.38%) and between 5/60 to 6/24 were 4 (12.90%). After giving injection bevacizumab patient was reviewed at 2 weeks, 4 weeks, 2months, 3months and 4 months. After giving injection avastin there was no improvement in 22 patients at 2 weeks. A maximum improvement of 2 lines on the Snellen chart was observed at 12 weeks in Classic and Occult CNVM patients, consistent with findings from the study by Geitzenauer W et al. in KlinMonatsblAugenheilkd.[17,18] Macular thickness by OCT before injection in classic CNV between 150-200µ there was 1 patient, 201-250µ 2 patients , 251-350µ 13 patients and more than 350µ there were 7 patients. Macular thickness by OCT before injection in occult CNV between 150-200µ there was 2 patients, 201-250µ 3 patients, 251-350µ 2 patients and more than 350µ there was 1 patient.

The base line mean macular thickness in CNV cases was 345µ. After injection about 69.56% of Classic CNV and 62.5% of Occult CNV showed reduction in macular thickness of 50µ at the end of 1month, and 52.17% of classic CNV and 37.5% occult CNV showed reduction of 100µ at the end of 4months. 1 case of Classic CNV showed no improvement till the end of the study because of macular scarring.

Table 1: Visual acuity by Snellens chart prior to injection Bevacizumab

Visual Acuity	No. of patients
HM-1/60	12
2/60-4/60	15
5/60-6/24	4

Table 2: Macular thickness by stratus OCT before injection Bevacizumab

OCT	Classic CNV	Occult CNV
100-150 µ	-	-
150-200 µ	1	2
200-250 µ	2	3
250-350 µ	13	2
>350 µ	7	1

Table 3: Vision improvement after injection Bevacizumab in Classic CNV

Vision improvement	2 weeks	4 weeks	2 months	3 months	4 months
No change	22	7	1	1	1
1 line improvement	1	10	15	10	8
2 lines improvement	-	6	6	11	13
>2 line improvement	-	-	1	1	1

Table 4: Vision improvement after injection Bevacizumab in occult CNVM

Vision improvement	2 weeks	4 weeks	2 months	3 months	4 months
No change	7	3	2	1	-
1 line improvement	1	4	2	3	1
2 lines improvement	-	1	2	2	5
>2 line improvement	-	-	2	2	2

Table 5: Reduction of macular thickness after injection Bevacizumab in Classic CNV

Macular Thickness reduction	2 weeks	4 weeks	2 months	3 months	4 months
Upto 50 µ	17	16	14	10	5
51- 100 µ	2	3	6	7	12
101- 150 µ	-	-	1	3	4
151- 200 µ	-	-	-	1	1
>200 µµµ	-	-	-	-	-
No change	3	3	2	2	1

Table 6: Reduction of macular thickness after injection Bevacizumab in Occult CNV

Macular thickness	2 weeks	4 weeks	2 months	3 months	4 months
Upto 50 µ	6	5	2	2	1
51- 100 µ	1	2	5	4	3
101- 150 µ	-	-	1	1	2
151- 200 µ	-	-	-	1	2
>200 µµµ	-	-	-	-	-
No change	1	1	-	-	-

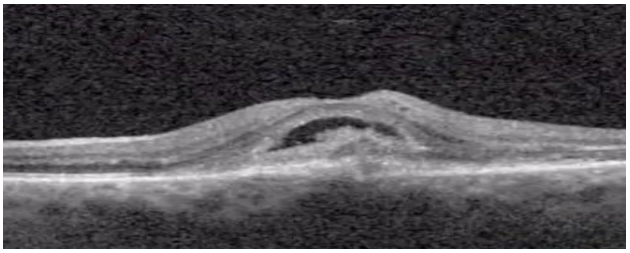

Figure 1: Type 2 CNV complex

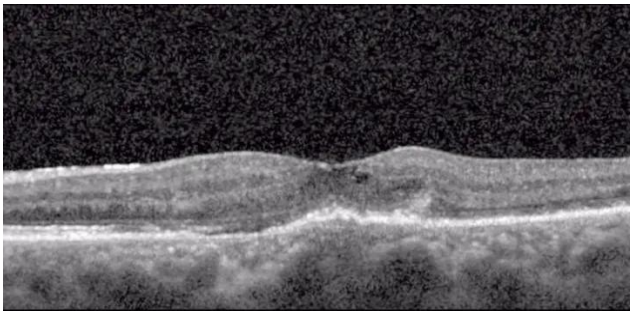

Figure 2: 4 weeks after 1st Anti-VEGF injection
(Regression of CNV complex, residual inraretinal cysts)

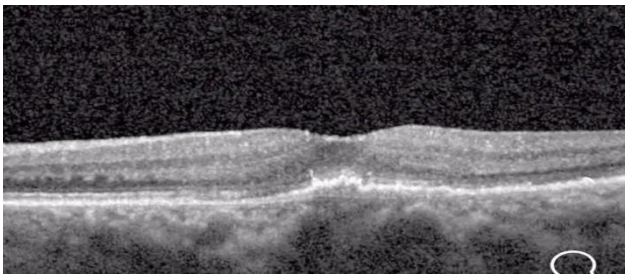

Figure 3: After loading 3 monthly dose
(no intraretinal or subretinal fluid)

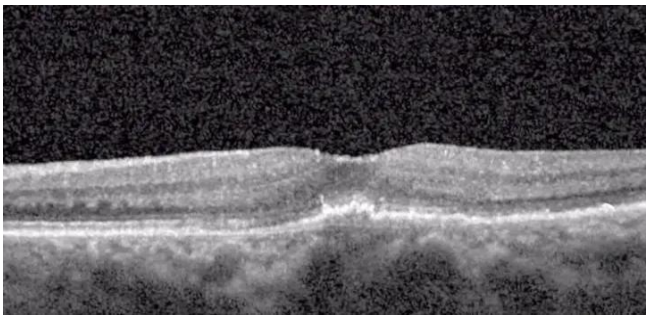

Figure 4: 8 weeks after Anti-VEGF

4. Discussion

Geographic atrophy and CNVM are characteristics of advanced ARMD, but drusen and RPE pigmentation are indicators of early ARMD, according to the International Age-Related Maculopathy Epidemiological Study Group.[18] High fat intake, smoking, high blood pressure, being a woman, and exposure to sunlight are all considered risk factors for ARMD. Treatment options for exudative ARMD include argon laser photocoagulation, photodynamic therapy, and anti-VEGF medications, with the last being especially important.[19] Assessing the improvement in visual acuity and the decrease in macular thickness in the aforementioned situations following intravitreal injection was the main objective.

The objective of this 4-month prospective, non-randomized clinical trial is to assess intravitreal bevacizumab's safety and effectiveness in treating neovascular AMD. Ten of the 31 patients that fulfilled the study's inclusion requirements were female, with a male to female ratio of 2.1:1. The average age was 55. With HM having the lowest V/A and 6/24 having the highest, the mean baseline pre-procedure V/A taken into consideration was 3/60. The mean macular thickness at baseline was 356µ. Following an explanation of the technique and the acquisition of consent, each patient received an intravitreal injection of 1.25 mg of bevacizumab under aseptic settings. The duration of the follow-up was 2–16 weeks. The 12-week follow-up was completed by all 31 patients. Improvements in macular thickness and visual acuity at every visit

5. Conclusions

Over the course of four months, intravitreal bevacizumab (1.25 mg) was well tolerated and showed notable safety and effectiveness. Because it was approved by the FDA and was less expensive than other anti-VEGF medicines, bevacizumab was chosen.

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