

Gholamhossein Yaghoobi* and Abbas Ataei Kachuei

Department of ophthalmology, Birjand University of Medical science, Valiaser Hospital, Ghafari St, South Khorassan, Birjand, Iran

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*Corresponding author: Gholamhossein Yaghoobi, Department of ophthalmology, Birjand University of Medical science, Valiaser Hospital, Ghafari St, South Khorassan, Birjand, Iran, Tel: 985614443001; Fax: 985614445402; E-mail: Yaqubig@yahoo.com

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Research Article

Intravitreal Bevacizumab Injection Effect in Exudative Age Related Macular Degeneration

Abstract

Exudative age-related macular degeneration is the most common cause of vision loss of people over the age 60 in the developed countries. The cause is not clear yet, but since Avastin is largely used for the treatment, therefore, this study was conducted to assess the influence of avastin.

Methods: All the 76 patients with exudative age-related macular degeneration came under intravitreal bevacizumab injection by an ophthalmologist with 1/25 mg in 0/05 ml. The second and third injections were repeated one month after the first injection. Patients were followed up one week, one month, and then in the third and sixth months after treatment. All patients had eye examination including visual acuity, slit lamp assessment (Slit-Lamp), intra ocular pressure and fundus examination.

Results: Visual acuity was 0/906±0/080 in patients before the study, a month after the injection 0/818 ± 0/097, and 3 months and 6 months after injection were 0/677± 0/126 and 0.488±0.164, respectively. The average difference in measured visual acuity was significant in all cases before injections, one month after injection, 3 months and 6 months after injection. (p<0.001).

The only complication observed during this study was mild temporary anterior uveitis in two patients (2/631%).

Conclusion: Intravitreal injection of bevacizumab showed improvement in vision during this study within 6 months. The cost effectiveness of bevacizumab and no systemic side effect except for only two patients with mild temporary uveitis were the main finding.

Introduction

Visual abilities of human eyes acts as means of complex optical and receiver system. The retinal tissue is a highly organized structure, capable of processing visual information to the brain via the optic nerve. Cone and rod photoreceptors turn into the optic nerve impulse. Photoreceptors are located in such a way that the cone cells are dense in the macula [1,2]. Age-related macular degeneration (AMD) affects the central vision in a way that it leads to a significant irreversible visual impairment. Both eyes are often affected, but the severity may vary. AMD is the most common cause of vision loss in people over 60 years old in developed countries. Sometimes AMD can occur in people under 40 years [3]. It is wrong that affected people are older. The study on American women of 50 years old showed the risk of the disease is four times more than breast cancer [4,5].

Visual acuity disturbance of AMD which is not a part of the natural process of AMD is divided in two groups; exudative age-related macular degeneration (eAMD) and non-exudative AMD. Severe visual loss from AMD is usually in people who have eAMD or geographic atrophy [3]. The main symptom of eAMD usually begins with sudden vision loss [2].

Despite the high prevalence of AMD, the causes are not clear yet. But the allele of genes on the some chromosomes is predisposing factors and the rule of antioxidants may have a protective role against AMD in the carotenoid family of compounds [6].

The incidence of AMD is different among different races; an indication of the role of race in the development of AMD. Moreover,

aging increases the risk of AMD. Other possible risk factors for the disease are positive family history, smoking, alcohol use, diabetes, high blood pressure, light-colored iris, high cholesterol, cardiovascular disease and female sex [7]. Retinal ischemia causes the secretion of a substance called Vascular Endothelial Growth Factor (VEGF) which may result in the emergence of new vessels, causing bleeding and retinal neovascularization and subsequent visual loss. Therefore, the inhibition of this factor could prevent the retinal and vitreous hemorrhage and the accompanying visual loss.

Studies have shown that VEGF is a major stimulus of angiogenic factor of neovascularization in AMD [8-10]. Inhibition of VEGF thereby prevents neovascularisation which in turn, decreases vascular permeability and thus, it would be an effective treatment in case of eAMD. Anti-VEGF drugs are currently used for the treatment of eAMD [11]. This investigation was conducted to reveal the effects of intravitreal injection of bevacizumab in patients with eAMD as a much more available among anti-vascular endothelial growth factors.

Methods

All patients referred to the eye clinic with eAMD were enrolled in the study. The patients' age were 65 years or older, with no history of previous treatment. The patients were experiencing angiographic evidence of leakage, an increase in the thickness of macula on Optical Coherence Tomography (OCT), new bleeding under the retina and visual acuity decline.

The visual acuity of patients was measured by Snellen chart and converted to the logarithm of Minimum Angle Resolution (log

MAR) and recorded before intervention. Patients who were not able to detect optative on snellen chart but had light perception or hand motion recognition, on a contract basis, were accepted as MAR3 and those patients with no light perception were considered as a conventional non-recognition log MAR 4. Eye drops were used under local anesthesia in an operating room after washing the eyelids and eyebrows with iodine 10% solution and 5% povidone-iodine. The intravitreal injection was performed by an ophthalmologist with using sterile vials of bevacizumab with prepared dosage of 1.25 mg/0.05 ml on the same day in a 30 gage insulin syringe needle. The second and third injections were repeated one month after the first injection.

Ophthalmic examination was carried out on the first day, one week and one month later respectively, then in the third month and the sixth month after the intervention. Ocular findings included patient's visual acuity, uveitic, endophthalmitis, lens opacity, funduscopy and fluid viewing on OCT. Re-treatment criteria were subretinal fluid, blood into the retina, decreasing visual acuity, fluorescein leakage and choroidal neovascularization. Patient who persistent the re-treatment criteria also known as failed to treatment and changed the treatment approach.

The data were entered in SPSS 15 software. The description data were illustrated by frequency distribution charts and the analysis were done by the Kolmogorov-Smirnov test in order to find the normality of the data. In a normal distribution analysis of variance within the groups the post hoc Bonferroni test was used. If the data were not in accordance with normal distribution and their levels were not significant, the Friedman test was used. The level of $P < 0.05$ was considered significant. This study after obtaining permission from the ethics committee, was implemented in research and clinical trials registration system.

Results

Almost a thirty (39/5%) of participating patients in the study were male and 46 (60/5) of patients were females. The average age of participants in the study was $74/38 \pm 10/16$.

According to **Tables 1,2** the mean difference was significant in all cases measured visual acuity before injections, one month, 3 months and 6 months after injection ($P < 0.001$).

Based on the above tables, only a temporary mild uveitis was observed which had a good response to topical steroid.

Table 1: Bonferroni test results according to mean difference in measured visual acuity before injections, one month, 3 months and 6 months after injection.

Variable	V/A Log MAR after injection in months	Mean	SD	P-Value
Before injection with	1	0.088	0.013	$P < 0.001$
	3	0.229	0.017	$P < 0.001$
	6	0.418	0.22	$P < 0.001$
After one month with	3	0.141	0.011	$P < 0.001$
	6	0.330	0.019	$P < 0.001$
After three month with	6	0.189	0.015	$P < 0.001$

VA; Visual acuity.

Table 2: The prevalence of ocular and systemic side effect of bevacizumab injection.

Complication	Frequency	Percent/%
Systemic	No	0
Uveitis	2	2/63
Total	2	2/63

Discussion

This study showed significant improvement of visual acuity after Bevacizumab intravitreal injection, compared to baseline visual acuity. ($P < 0.001$). Similar results have been reported in a study by Hyun Seung and colleagues. They concluded that in a total of 103 eyes of 89 patients with subfoveal neovascularization after two years of following up, 24 eyes have recurrence and the remainder had stable condition. They concluded that bevacizumab monotherapy in the treatment of myopic subfoveal neovascularization has an effective role. Although, they had 23/3% recurrence rate after two years of follow-up [11], in our study we did not have any recurrence during the six months follow-up. So this difference could be the result of our short duration of follow up.

In a retrospective study in 2007-2006 by Jaime Levy and colleagues, 65 patients with wet AMD were treated with intravitreal injection of bevacizumab. After 6 months of follow up, the mean visual acuity changed from a baseline 1.12 ± 0.62 to 0.83 ± 0.47 ($P < 0.001$). They also could not find any side effects of avastin in study groups [12].

In a prospective study in 2013 by Dalia Sabry and his colleagues, the mean logMAR was 1.43 before treatment, but 6 months after treatment, it significantly improved the patients' vision to 0.7 logMAR ($P: 0.02$) but statistically significant correlation was not observed between the recovery of visual acuity and number of intraocular injection [13]. In another study by Mahmood S et al., the effect of intravitreal injection of bevacizumab was also shown to have dependency on the duration of wet macular degeneration. Interestingly, we obtained similar results in our experiments [14]. Among the subjects of our study, the only side effect was eye inflammation in 2 patients (2/631 percent). The study by Ozkaya and colleagues in 2013 in newly diagnosed patients with eAMD, observed uveitis in 5 (%6.3) and those treated with bevacizumab were 2 cases (%2.7). Since this side effect is seen in this study and ours, further investigation is needed [15].

None of the subjects in our study became potentially blind during the six months follow up. Chong and his colleagues demonstrated that bevacizumab compared to Ranibizumab in the treatment of eAMD is more cost-effective but Ranizumab half life is lower and needed monthly injection. Bevacisumaub does not require monthly injections but there are several reported cases of blindness worldwide but no any patient in our study developed sight threading complication. The risk of systemic and ocular side effects and the cost-effectiveness of these drugs in affected eyes are puts more emphasis on research so that their side effects are constantly monitored [16]. In some other research, intravitreal injection of bevacizumab in the 6-month follow-up was effective in the treatment of neovascularization without any side effects [13].

Conclusions

Avastin improved the patients' visual acuity within 6 months of treatment. It did not show any systemic side effects during the six months follow-up. Only two patients developed uveitis, a none threatening visual side effect that response to topical steroid treatment after intravitreal injection, and hence, monitoring this therapeutic agent and its side effects in the control and treatment of age-related macular degeneration is important due to their cost effectiveness versus other expensive anti-vascular endothelial growth factors.

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