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Original Research Article

Assessment of Safety Profile of Intravitreal Bevacizumab in Ocular Lesions

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Abstract

Background: Diabetic macular edema (DME), age-related macular degeneration (AMD), and retinal vein occlusion (RVO) are the major etiologic factors of visual impairment and loss of central vision worldwide. The present study was conducted to assess safety profile of intravitreal bevacizumab in ocular lesions.

Materials & Methods: 78 patients of visual impairment of both genders was included. Injection bevacizumab was performed performed by a vitreoretinal fellow under all aseptic precautions using a single 26-G needle prick technique. Patients were evaluated at baseline and post-injection at day 7 and 4 weeks. SD-OCT was repeated at 4 weeks after each injection. ICG and DFA were repeated according to the condition of the disease and at the discretion of treating physician.

Results: Common conditions were diabetic macular edema in 27, age related macular degeneration in 8, branched retinal vein occlusion in 6, central retinal vein occlusion in 10, vitreous hemorrhage in 5, polypoidal choroidal vasculopathy in 7, submacular hemorrhage in 7 and neovascular glaucoma in 8 patients. The difference was significant ($P< 0.05$). The mean injections required in diabetic macular edema was 2.98, in age related macular degeneration was 1.12, in branched retinal vein occlusion was 2.04, in central retinal vein occlusion was 2.11, in vitreous hemorrhage was 1.42, in polypoidal choroidal vasculopathy was 1.36, in submacular hemorrhage was 1.10 and in neovascular glaucoma was 1.02. Common adverse events were endophthalmitis in 3 and intraocular pressure rise in 5 cases. The difference was non- significant ($P> 0.05$).

Conclusion: Bevacizumab is a safe and economical pharmacotherapeutic agent that is used to treat a various ocular disorders.

Keywords: Bevacizumab, ocular disorders, submacular hemorrhage

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Introduction

Diabetic macular edema (DME), age-related macular degeneration (AMD), and retinal vein occlusion (RVO) are the major etiologic factors of visual impairment and loss of

central vision worldwide.[1] The management of these retinal disorders has been developing gradually over a period.[2] Intravitreal injections have transformed the treatment of common retinal diseases, including neovascular age-related macular degeneration (AMD), diabetic retinopathy, and retinal vein occlusions (RVOs). Furthermore, favourable results were reported with intravitreal injection of anti-VEGF agents for various other ocular diseases, such as neovascular glaucoma, retinopathy of prematurity and intraocular tumors.[3]

Bevacizumab was designed to inhibit tumor angiogenesis is approved to be used in colorectal carcinomas. Successively, it expanded widespread access as an off-label medication for the treatment of various neovascular disorders. Nonetheless, as bevacizumab is a chemotherapeutic agent, it is presently available in a 4-mL vial from which multiple doses are used as aliquots for ophthalmic use.[4]

Bevacizumab is noninferior to ranibizumab with a comparable safety profile. In the American Society of Retina Specialists Preferences and Trends Survey conducted in 2015, which was on the basis of the existing body of literature and taking into account the cost-effectiveness of bevacizumab, 64% of the US retinal physicians used bevacizumab as the first-line treatment for AMD and >80% of the US members treated choroidal neovascularization from histoplasmosis and other non-AMD causes with bevacizumab.[5] The present study was conducted to assess safety profile of intravitreal bevacizumab in ocular lesions.

Materials & Methods

The present study comprised of 78 patients of visual impairment of both genders. The consent was obtained from all enrolled patients.

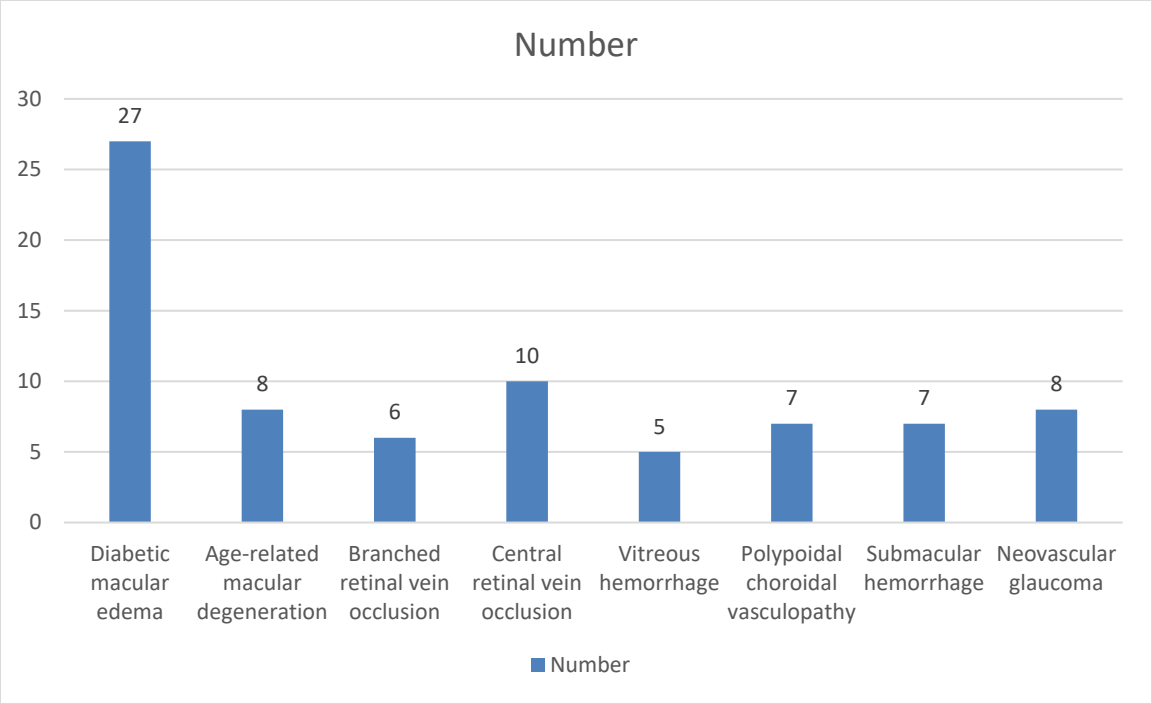
Data such as name, age, gender etc. was recorded. The patient underwent routine ophthalmic examination including best corrected visual acuity, intraocular pressure (IOP) evaluation by Goldmann applanation tonometry, slit-lamp biomicroscopy, indirect ophthalmoscopy, and spectral domain optical coherence tomography (SD-OCT). Injection bevacizumab was performed performed by a vitreoretinal fellow under all aseptic precautions using a single 26-G needle prick technique. Patients were evaluated at baseline and post-injection at day 7 and 4 weeks. SD-OCT was repeated at 4 weeks after each injection. ICG and DFA were repeated according to the condition of the disease and at the discretion of treating physician. Data thus obtained were subjected to statistical analysis. P value < 0.05 was considered significant.

Results

Table 1: Intravitreal injections for ocular condition

Conditions	Number	P value
Diabetic macular edema	27	
Age-related macular degeneration	8	
Branched retinal vein occlusion	6	
Central retinal vein occlusion	10	
Vitreous hemorrhage	5	
Polypoidal choroidal vasculopathy	7	
Submacular hemorrhage	7	
Neovascular glaucoma	8	

Table I, graph I shows that common conditions were diabetic macular edema in 27, age related macular degeneration in 8, branched retinal vein occlusion in 6, central retinal vein occlusion in 10, vitreous hemorrhage in 5, polypoidal choroidal vasculopathy in 7, submacular hemorrhage in 7 and neovascular glaucoma in 8 patients. The difference was significant (P< 0.05).



Fiure 1: Intravitreal injections for ocular condition

Table 2: Mean number of injections based on ocular pathology

Conditions	Mean	P value
Diabetic macular edema	2.98	0.01
Age-related macular degeneration	1.12	
Branched retinal vein occlusion	2.04	
Central retinal vein occlusion	2.11	
Vitreous hemorrhage	1.42	
Polypoidal choroidal vasculopathy	1.36	
Submacular hemorrhage	1.10	
Neovascular glaucoma	1.02	

Table II, graph II shows that mean injections required in diabetic macular edema was 2.98, in age related macular degeneration was 1.12, in branched retinal vein occlusion was 2.04, in central retinal vein occlusion was 2.11, in

vitreous hemorrhage was 1.42, in polypoidal choroidal vasculopathy was 1.36, in submacular hemorrhage was 1.10 and in neovascular glaucoma was 1.02. The difference was significant (P< 0.05).

Table 3: Assessment of adverse events

Adverse events	Number	P value
Endophthalmitis	3	0.14
Intraocular pressure rise	5	

Table III shows that common adverse events were endophthalmitis in 3 and intraocular pressure rise in 5 cases. The difference was non- significant (P> 0.05).

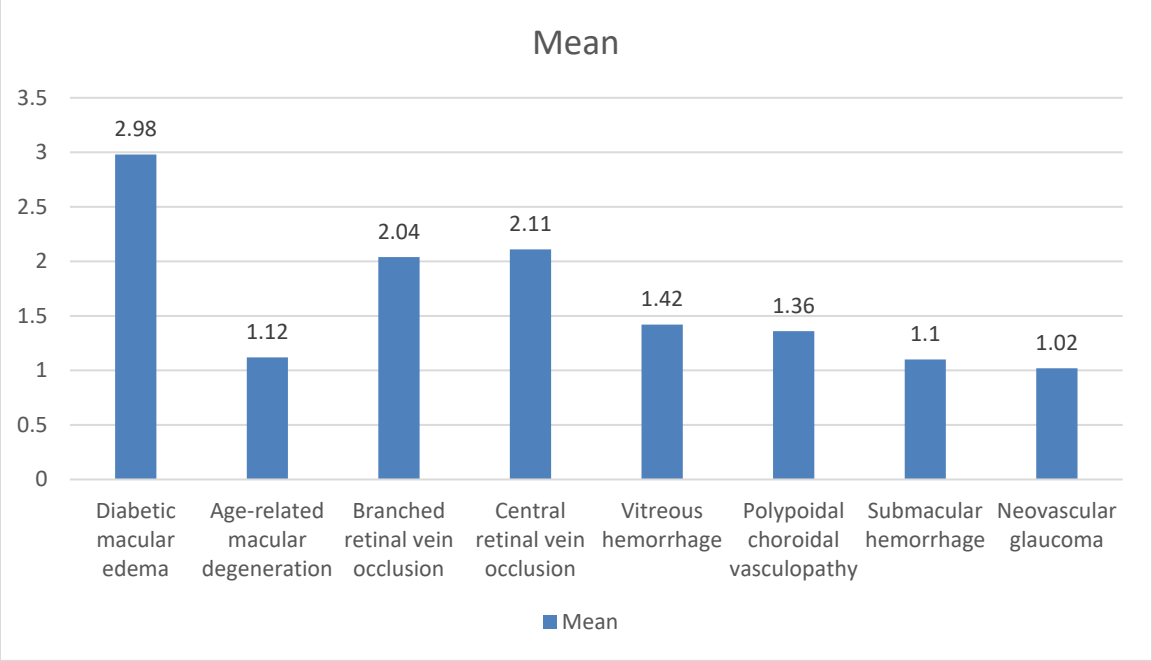


Figure 2: Mean number of injections based on ocular pathology

Discussion

Bevacizumab was first time used in 2005. Successively, multiple anti-VEGF agents such as pegaptanib sodium, ranibizumab and aflibercept have been established for the management of various ocular indications such as AMD, DME, and RVO.[6] Characteristically, the patients with retinal diseases such as AMD and DME need multiple doses of anti-VEGF agents.[7] As the burden of injections is high in many of these retinal pathologies, few pertinent questions still remain regarding the treatment such as the choice of agent, and the economic burden of therapy.[8] Ranibizumab and aflibercept have been approved by the US Food and Drug Administration (FDA) for the treatment of these retinal diseases.[9] The present study was conducted to assess safety profile of intravitreal bevacizumab in ocular lesions.

We found that common conditions were diabetic macular edema in 27, age related macular degeneration in 8, branched retinal vein occlusion in 6, central retinal vein occlusion in 10, vitreous hemorrhage in 5, polypoidal choroidal vasculopathy in 7,

submacular hemorrhage in 7 and neovascular glaucoma in 8 patients. Jain et al[10] in their study 3806 injections of 1761 patients that were administered with intravitreal bevacizumab injection at a tertiary eye care center in India. The injections were administered on a pro re nata basis for various indications such as age-related macular degeneration (AMD), diabetic macular edema (DME), and retinal vein occlusion (RVO). The mean age of the patients was 61.8 ± 11.59 years. A total of 59.2% of the patients were men and 40.8% women. The most common indications for which the injection was administered were DME (27.5%), AMD (26%), and branch RVO (12.3%). Among the ocular side effects, endophthalmitis was seen in three eyes (0.08%), retinal breaks in none of the eyes whereas 35 eyes had a rise in intraocular pressure (IOP) >21 mmHg (0.9%). Pre-existing glaucoma was present in four eyes while remaining 31 eyes did not have any history of glaucoma. IOP rise was significantly more in eyes with pre-existing glaucoma as compared to non-glaucomatous eyes (P = 0.04). No systemic adverse events were noted in our study population.

We observed that mean injections required in diabetic macular edema was 2.98, in age related macular degeneration was 1.12, in branched retinal vein occlusion was 2.04, in central retinal vein occlusion was 2.11, in vitreous hemorrhage was 1.42, in polypoidal choroidal vasculopathy was 1.36, in submacular hemorrhage was 1.10 and in neovascular glaucoma was 1.02. A study conducted on 146,942 Medicare beneficiaries did not show any difference in the risk of mortality, heart attack, stroke, or bleeding among the patients with AMD treated with bevacizumab or ranibizumab.[11]

We found that common adverse events were endophthalmitis in 3 and intraocular pressure rise in 5 cases. Van Der Reis et al[12] concluded that the rates of serious ocular and systemic ADRs after anti-VEGF injections applied for any ophthalmic indication were very low, without any differences in the incidences among the assessed drugs. It was observed that systemic adverse events had lower incidence rates for intravitreal bevacizumab in comparison with ranibizumab.

Conclusion

Authors found that Bevacizumab is a safe and economical pharmacotherapeutic agent that is used for treating a variety of ocular disorders.

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