

Indications for Intravitreal Bevacizumab in Ibadan, Sub-Saharan Africa

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Abstract: *Background:* Angiogenesis is a contributing factor in some retinal diseases, hence the role of vascular endothelial growth factor (VEGF) as a common pathway in proliferative retinopathies. Bevacizumab has been found to be effective in the treatment of these diseases.

The aim of this study was to review all cases of intravitreal bevacizumab given in the retinal unit of the University College Hospital, Ibadan from July, 2010 to June 2012, pointing out the common indications.

Methods: After obtaining ethical approval from the University College Hospital/University of Ibadan Review Board for the study, all cases of intravitreal injections of bevacizumab recorded in the retinal register during the study period (July 2010 to June 2012) were retrieved. Age, sex, diagnoses and indication for injection were recorded in the data sheet prepared for the study. Results were analyzed using proportions and percentages.

Results: A total of one hundred and thirty four injections of bevacizumab were given in the study period. The most common indication was cystoid macular edema from retinal vein occlusion ([26(19.4%)] followed by wet age related maculopathy [23(17.1%)] and sickle cell retinopathy [(22(16.4)]. Emerging indications included idiopathic polypoidal choroidal vasculopathy [8(6%)] and retinal macroaneurism with macular edema [6(4.5%)].

Conclusion: Cystoid macular edema from vascular occlusion and wet age related macular degeneration are the major indications for intravitreal bevacizumab injection in Ibadan.

Keywords: Cystoid macular edema, intravitreal bevacizumab, retinal vein occlusion, sickle cell retinopathy.

INTRODUCTION

Angiogenesis is a contributing factor in many diseases, hence the role of vascular endothelial growth factor (VEGF) as a common pathway in proliferative retinopathies such as diabetic retinopathy [1] and sickle cell retinopathy [2]. It is an important pathogenetic mechanism in diabetic macular edema [3], neovascular age-related macular degeneration (AMD) [4], cystoids macular edema (CME) from retinal vascular occlusions [5] and retinopathy of prematurity (ROP) [6]. It is also implicated in neovascular glaucoma [7]. VEGF is responsible for endothelial cell proliferation, vascular permeability and ocular inflammation [8]. Ranibizumab and Bevacizumab are both antibodies to VEGF and have been shown to be effective in the management of macular edema and vasoproliferative retinal diseases [9-11].

In developing nations like Nigeria, bevacizumab is preferred to ranibizumab, in view of the cost of the latter. However, the former is used as an off label drug. The recent CATT trial (Comparism of Age related maculopathy Treatment Trial) has demonstrated that both medications have equal efficacy [12]

The aim of this study was to review all cases of intravitreal bevacizumab given in the retinal unit of the

university college hospital, Ibadan from July 2010 to June 2012, pointing out the common indications.

METHODS

After obtaining ethical approval from the University College Hospital/University of Ibadan Review Board for the study, all cases of intravitreal injections of Bevacizumab recorded in the retinal register during the study period (2010-2012) were retrieved. Age, sex, diagnoses and indication for injection were recorded in the data sheet prepared for the study. Results were analyzed using proportions and percentages.

Method of injection: The injection is usually done in the sterile theater environment. After an informed consent, topical tetracaine hydrochloride 0.5% was instilled to the eye. 1.25 mg of bevacizumab in 0.05 ml was given intravitreally 4 mm from the limbus in the infero temporal quadrant. Anterior chamber paracentesis was done to reduce the intraocular pressure. Topical Povidone Iodine 5% was instilled before and after the injection. The patient was reviewed first day post injection, one week and monthly. Slit lamp examination and the intraocular pressure were checked at each visit.

RESULTS

A total of one hundred and thirty four injections of bevacizumab were given in the study period. The most common indication was cystoid macular edema from retinal vein occlusion followed by wet age related macular

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Table 1. Indications for intravitreal bevacizumab in Ibadan, Sub-Saharan Africa.

Indications/Age (Yrs)	<30	31-40	41-50	51-60	60+	Total (%)
Retinal Vein Occlusion + CME	-	-	2	7	17	26 (19.4)
Wet AMD	-	-	2	4	17	23 (17.1)
Sickle cell Retinopathy + Vit. Heam.	4	11	3	4	-	22 (16.4)
Prolif Diabetic Retinopathy +Vit Haem	-	-	4	3	6	13 (9.7)
Diabetic Macular Edema	-	-	2	2	6	10 (7.5)
Branch Retinal Vein Occlusion + Vit. Haem.	-	-	2	1	7	10(7.5)
Idiopathic Polypoidal Choroidal Vasculopathy	-	-	1	2	5	8(6.0)
Idiopathic CNVM	-	-	6	-	1	7(5.2)
Neovascular Glaucoma	-	-	2	3	2	7(5.2)
Retinal arterial macroaneurism	-	-	-	4	2	6(4.5)
Others	1	-	-	1	-	2(1.5)
Total	5	11	24	31	63	134(100)

CME= cystoid macular edema; AMD= age related macular degeneration; CNVM= choroidal neovascular membrane; Vit. Heam= vitreous haemorrhage; Prolif= proliferative.

degeneration (AMD) and sickle cell retinopathy among others (Table 1).

DISCUSSION

The most common indication for intravitreal bevacizumab in Ibadan was retinal vein occlusion with macular edema. Retinal vein occlusion is a common presentation to the retinal clinic of the University College Hospital, Ibadan [13]. This may be due to the fact that systemic hypertension, a strong predisposing factor for retinal vein occlusion is on the rise in Nigeria and is the most common medical presentation among Nigerians [14] with the prevalence between 11.2% [15] and 25% [16-18]. As retinal vein occlusion is associated with increased levels of Vascular Endothelial Growth Factor (VEGF), macular edema from retinal vein occlusion has been reported to respond well to intravitreal bevacizumab [19]. Grid laser treatment showed visual acuity benefit in branch retinal vein occlusion [20]. Intravitreal triamcinolone acetamide demonstrated transient inconsistent benefit with potential complications [21]. Intravitreal bevacizumab appears to be a safe and effective treatment for macular edema associated with branch retinal vein occlusion, at least in the short term [22-26].

The second common indication for bevacizumab injection was wet age related macular degeneration (AMD). Age related macular degeneration is a significant presentation in Ibadan, sub-Saharan Africa as shown by a recent study [27]. In the western world and Asia, it is the most common indication [28]. Bevacizumab is equally effective as ranibizumab for producing visual improvement as opposed to previous treatments that either stabilizes vision or made vision worse [29].

Sickle cell retinopathy is a significant cause of retinal disease in Ibadan, West Africa. The prevalence of the hemoglobin S gene in Nigeria is between 20 and 25% [30, 31]. In Nigeria, Hemoglobin SC produces most of the retinopathic changes with previous studies showing patient's presentation at the late stages of the disease [32-34].

Intravitreal bevacizumab help in clearing vitreous hemorrhage before the administration of adequate laser treatment.

Diabetic retinopathy with vitreous hemorrhage and macular edema are emerging indications in Ibadan. There is a global trend towards increase of the incidence and prevalence of diabetes in Africans due to changing lifestyles [35]. Diabetic retinopathy is now a significant cause of blindness in Nigeria [36, 37]. In June 2010, the diabetic clinical research network (DCRNet) compared the anti VEGF ranibizumab with laser and triamcinolone in a randomised trial and found ranibizumab (at a dose of 0.3 mg) to be superior to both laser and triamcinolone either alone or in combination with laser [38]. The RESTORE study showed that Ranibizumab monotherapy or combined with laser provided superior visual acuity gain over standard laser in patients with visual impairment due to diabetic macular edema (DME) [39]. The RESOLVE Study and the READ 2 study also clearly showed that ranibizumab is effective in producing visual gain [40, 41]. Bevacizumab (at a dose of 1.25 mg), an antiVEGF similar to ranibizumab has also been found to be superior to laser in The BOLT study [42].

Idiopathic polypoidal choroidal vasculopathy (IPCV) is an emerging diagnosis in our center. A study from our center describes the disease as more common in women, presenting with hemorrhagic pigment epithelial detachment (PED) subretinal and breakthrough vitreous hemorrhage [43]. Intravitreal bevacizumab help reduce the height of PED and reduces exudation and hemorrhage but the definitive treatment is Photodynamic therapy (PDT) [44].

Other indications found in the study included Idiopathic choroidal neovascular membrane (CNVM), myopic CNVM, neovascular glaucoma and retinal arterial macroaneurism with exudation involving the macula. All these have been reported to respond well to bevacizumab [45, 46]. We also encountered a case of Coats' disease with massive exudation in a young man. Intravitreal Bevacizumab has been reported to help reduce exudation in coats [47].

Procurement and dispensing bevacizumab in developing countries are challenging. A 4 ml vial is 5 times the minimum wage of a worker in Nigeria. The options available include pooling patients together for the injection, however in small centers, the number of patients available may not justify purchasing a vial. The other option is to involve the pharmacy department of the hospital concerned to dispense in tuberculin syringes under strict aseptic process. The risk of endophthalmitis is significant with this option and need to be seriously considered. It is important to remember the cold chain involvement in the dispensing of bevacizumab. Frequent power outages in developing nations may disrupt this chain rendering the drug ineffective. The use of alternative power supply is imperative.

CONCLUSION

The most common indications for intravitreal bevacizumab in Ibadan from this study included cystoid macular edema from retinal vein occlusion, wet age related macular degeneration and sickle cell retinopathy. In developing countries, eye centers should bear in mind the challenges of dispensing bevacizumab.

LIMITATIONS

The study being a retrospective study, may be limited by accurate data retrieval from case records.

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CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

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