Brief Communication

Acute Endophthalmitis after Intravitreal Bevacizumab Injections at The Tertiary Centre in Nepal

Eli Pradhan[1], Sushma Duwal[1], Sanyam Bajimaya[1], Raba Thapa[1], Sanjita Sharma[1], Anu Manandhar[1], Manish Poudel[1], Govinda Paudyal[1]
[1]Tilganga Institute of Ophthalmology, Kathmandu Nepal

Abstract

Introduction: There are many reports of endophthalmitis following Anti-VEG F use in developed countries and from India, but there are none from Nepal yet. Therefore, the aim of this study was to report the prevalence and management of acute endophthalmitis after intravitreal injection of bevacizumab. **Methods:** This is a clinical, retrospective, non-comparative study, performed in Tilganga Institute of Ophthalmology, Kathmandu, Nepal from Jan 2015 till Dec 2016. All consecutive cases of intravitreal 1.25 mg of bevacizumab injections during the study period were collected from Bevacizumab registry of the operation theatre. A total number of endophthalmitis, following intravitreal bevacizumab injections were collected from Endophthalmitis registry. The statistical analysis was carried out by SPSS for percentage calculation and its 95% Confidence Interval (CI) calculation. **Results:** There were 4182 injections performed during the study period for various retinal conditions. Two eyes of two patients with acute postoperative endophthalmitis were identified in the first week following intravitreal injections of 1.25 mg bevacizumab among a total of 4128 injections with a prevalence of 0.048% (95% CI: 0.00 to 0.12.) **Conclusions:** The prevalence of acute endophthalmitis following intravitreal Bevacizumab in our retrospective series was 0.048% and was comparable with the other studies conducted elsewhere. Acute post-injection endophthalmitis following intravitreal bevacizumab can result in severe loss of vision. Therefore prompt recognition and treatment are important part of its management in such patients.

Introduction

Bevacizumab (Avastin, Genetech, San Francisco, CA) is a full length humanized monoclonal antibody against VEGF-A and has been approved as a systemic adjuvant treatment for metastatic colon cancer (Ferrara N et al, 2005).

Financial interest: Nil
Conflict of interest: Nil
Received: 12/07/2017 Accepted: 03/11/2017

Corresponding author
Dr Sushma Duwal, MD
Vitreo-retina surgeon,
Tilganga Insitute of Ophthalmology
Phone no: +977 9841403405
E-mail: duwalsushma@hotmail.com

The use of anti-vascular endothelial growth factor (anti-VEGF) agents has resulted in a dramatic increase in intravitreal injections in recent years (Ramulu PY et al, 2010). One of the severe complications is endophthalmitis, leading to severe visual loss inspite of prompt treatment (Schwartz SG et al, 2014).

Among different anti-VEGF, intravitreal bevacizumab (IVB) is available in our country, which is being increasingly used as an off-label treatment for common retinal diseases as in other countries (Ramulu PY et al, 2010; Schwartz SG et al 2014; Lyall DA et al, 2012; Day S et al, 2011)

There are many reports of endophthalmitis following Anti-Veg F use in developed countries and from India (Khan P et al, 2016), but there are none from Nepal yet.

Therefore, the aim of this study was to report the prevalence and management of acute endophthalmitis after intravitreal injection of bevacizumab.

Methods

This is a clinical, retrospective, non-comparative study, performed in Tilganga Institute of Ophthalmology, Kathmandu, Nepal from Jan 2015 till Dec 2016. All consecutive cases of intravitreal 1.25 mg of bevacizumab injection during the study period were collected from Bevacizumab registry of the operation theatre.

The cases that received IVB in combination with pars plana vitrectomy or phaco emulsification or other procedures were excluded. The Ethical committee of Tilganga institute of ophthalmology approved the study.

Bevacizumab is available in vials of 100 mg in 4 ml from which aliquots of the prerequisite dose of 1.25 mg/0.05 ml are prepared thus reducing the cost of one injection. The procedure of IVB was completed in absolutely aseptic and sterile condition in operation theatre after proper cleaning and draping of the eye. The injecting surgeon was also properly scrubbed with sterile surgical globes. The eye patch was removed after 4 hours of the procedure and discharged with topical Ofloxacin eye drops, four times a day with Ciprofloxacin eye ointment at night for 1 week. The patients were advised for follow up in 4 weeks unless there was any concern. In cases of severe pain and blurred vision, they were requested to attend emergency as soon as possible.

A total number of endophthalmitis, following intravitreal Bevacizumab injections were collected from Endophthalmitis registry. The statistical analysis was carried out by SPSS for percentage calculation and it's 95% Confidence Interval (CI) calculation.

Results

There were consecutive 4182 IVB injections performed during the study period from Jan 2015 till Dec 2016. The different retinal conditions were diabetic macular edema, age related macular degeneration, macular edema due to branch retinal vein occlusion and central retinal vein occlusions and choroidal neovascular membrane due to various secondary causes.

Two eyes of two patients with acute postoperative endophthalmitis were identified in the first week following intravitreal injections of 1.25 mg bevacizumab among a total of 4128 injections with a prevalence of 0.048% (95% CI: 0.00 to 0.12.).

One case of endophthalmitis was culture negative and another one was culture-positive with organisms isolated being, staphylococcus aureus (Table 2). Early intervention was performed; including injection of intravitreal antibiotics, as well as pars plans vitrectomy (PPV) after clinical appearance of post-injection endophthalmitis. In both the cases, intravitreal injections were repeated twice, along with surgical procedure of PPV.

The culture negative was 61 years old male, hypertensive, and non- diabetic (Table 1) with the endophthalmitis occurring in 2nd dose of IVB on 3rd day of procedure. PPV was performed on 3rd day of presentation as endophthalmitis. Moreover, Vitreous tap and Intravitreal antibiotics were repeated on 2nd week before the inflammation subsided.

Likewise, the culture positive was 71 years old, female diabetic patient (Table 2), presented on 5th day after receiving the 4th dose of IVB. She underwent PPV on 2nd day of presentation as endophthalmitis.

Table 1: Best corrected visual acuity of patients before IVB, systemic illness and indications

Patient no	Gender	Age	Systemic association	Indication	BCVA+ before IVB in affected
1	Male	61	HTN*	Superior Macular BRVO	1/60
2	Female	71	DM#	Diabetic Macular edema	6/60

*HTN: Hypertension
#DM: Diabetes Mellitus
+BCVA: Best corrected visual acuity

Table 2: Best corrected visual acuity during presentation and after follow up with Culture report of Vitreous Tap

Patient no	BCVA at presentation in affected eye	BCVA after 6 months in affected eye	Culture report
1	PL, PR accurate*	3/60	No Growth
2	HM#	2/60	Staphylococcus aureus

*PL, PR: Perception of Light, Projection of Rays
#HM: Hand Movement

However, the final visual acuity was worse in both eyes, in 6 months follow up (Table 2) in-spite of improvement clinically. Nonetheless, none of the eyes developed phthisis bulbi or required enucleation.

Discussion

Bevacizumab (AVASTIN®, Genentech, Inc.) became the first therapy approved by the US Food and Drug Administration (FDA) designed to inhibit angiogenesis in cancer. After approval, bevacizumab gained access into ophthalmology, to treat various types of retinal and neovascular diseases.

The ocular and systemic side effects of Anti-VEGFs were addressed by a number of studies (Goldberg RA et al, 2012; Rasier R et al, 2009;Tatar O et al, 2009)

One of the main devastating complications of the bevacizumab intravitreal injection is endophthalmitis. Different reports are present about the incidence of the post-injection endophthalmitis (Artunay O et al, 2009; Mason JO et al, 2008)

A population-based study (Lyall DA et al, 2012) in the United Kingdom estimated the per-injection rate of endophthalmitis following intravitreal anti-VEGF injection to be 0.025 percent. A review of the United States Medicare claims database revealed a per-injection rate of 0.09 percent for endophthalmitis associated with intravitreal anti-VEGF injections (Day S et al, 2011)

Shimada H et al, 2013 suggested that endophthalmitis can be reduced to a minimum by preventing normal flora of the conjunctiva and bacteria in the oral cavity from entering the injection site by proper draping and irrigating conjunctiva with 0.25% povidone iodine, which is also the standard procedure that we do in our hospital set up.

The prevalence of endophthalmitis after intravitreal injection of bevacizumab in our retrospective study is comparable with other studies (Lyall DA et al, 2012; Day S et al, 2011; Mccanel CA et al, 2011).

Our study is limited due to its retrospective nature and absence of control arm. The other limitation could be underestimation of the incidence and prevalence of endophthalmitis

as all cases may not have presented at TIO, and we were not able to follow up each patient.

Therefore it suggests for prospective study and comparison of the results from different centers in Nepal, where facility of IVB is available.

Conclusions

The prevalence of endophthalmitis after intravitreal injection of bevacizumab in our retrospective study was 0.048% and was comparable with the other studies conducted elsewhere.

Acute post-injection endophthalmitis following intravitreal bevacizumab can result in severe loss of vision. Therefore prompt recognition and treatment are important part of its management in such patients.

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