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Incidence of acute endophthalmitis after intravitreal bevacizumab injection in a tertiary hospital

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ABSTRACT

Aims: To investigate the incidence of acute endophthalmitis after intravitreal bevacizumab injections.

Methods: Patients who received treatment with intravitreal bevacizumab (1.25 mg/0.05 ml) injections for various indications between November 2020 and March 2022 were included in this retrospective study. The patients were followed up for 4 weeks after the injection in terms of acute endophthalmitis symptoms and signs.

Results: Acute endophthalmitis developed in 1 patient after 4593 intravitreal bevacizumab injections were administered to 1427 eyes of 1026 patients, and the incidence was found to be 0.0217%. The patient who developed acute endophthalmitis underwent pars plana vitrectomy and after 3 months, a significant improvement in visual acuity was observed.

Conclusion: Development of endophthalmitis postoperatively was found to be moderately low after intravitreal bevacizumab injection. It was concluded that following asepsis rules and optimal bevacizumab preparation conditions could further reduce this.

Keywords: Bevacizumab, intravitreal injections, endophthalmitis, complications

INTRODUCTION

Bevacizumab (Avastin, Genetech inc., San Francisco, California, USA) is a recombinant human monoclonal antibody that can bind to all forms of vascular endothelial growth factor (VEGF).[1] It is an approved drug for the treatment of colorectal cancers.[2] However, despite being off-label it is also widely used intravitreally in the treatment of ocular diseases such as macular edema due to diabetic retinopathy (DRP), choroidal neovascularization (CNV), retinal vein occlusion (RVO), retinopathy of prematurity (ROP), age-related macular degeneration (AMD) and degenerative myopia.[3-7] Intravitreal bevacizumab (IVB) administration has ocular side effects such as subconjunctival hemorrhage, transient intraocular pressure (IOP), vitreous hemorrhage, and retinal detachment, as well as serious side effects that cause permanent vision loss such as acute endophthalmitis.[8,9]

With the worldwide increase in retinal diseases that cause vision loss, off-label use of intravitreal bevacizumab (IVB) is increasing, due to it being more cost-effective.[10] Risk factors for the development of post-injection acute endophthalmitis include immune system diseases, failure of physicians and auxiliary personnel to comply or pay attention to asepsis techniques, withdrawal of more than one dose of medication from a single vial, presence of chronic ocular infection in patients, and patients' failure to pay attention to post-procedural hygiene.[9] Asepsis training of physicians and auxiliary personnel and explaining hygiene rules to patients can reduce the risk of acute endophthalmitis that may occur after injection.

The aim of our study was to evaluate the incidence, management, and visual results of acute endophthalmitis after IVB injections in our ophthalmology clinic.

METHODS

The study was carried out with the permission of Gaziantep Islamic Science and Technology University Ethics Committee (Date: 07.06.2022, Decision No: 129.17.18). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

In this retrospective study, the records of 1026 patients who presented to our ophthalmology clinic with the complaint of low vision, who were treated with IVB (1.25 mg/0.05 ml) injection for various indications between November 2020 and March 2022, were retrospectively reviewed. Only patients who received IVB were included in the study.

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The best corrected and uncorrected visual acuities of all patients were measured with the Snellen chart, intraocular pressure status was measured with a Goldman applanation tonometer and anterior segment examinations were performed with slit lamp biomicroscopy. Fundus examination was performed with a 90-diopter lens. The retina and choroid were evaluated with optical coherence tomography (OCT, Optovue RTVue XR, Optovue Inc., Fremont, CA) and fundus fluorescein angiography (FFA, Topcon TRC-50DX, Topcon Corporation, Japan). Patients diagnosed with macular edema due to diabetic retinopathy, choroidal neovascularization and fluid due to AMD, and macular edema due to RVO were administered intravitreal bevacizumab injection at 1-month intervals. A separate vial is applied for each injection. All intravitreal injections were administered by 2 surgeons with 2 years of experience in this field (MB, GGS). Before the application, the surgeon and assistant nurse wore a surgical mask, cap, and surgical attire. Disposable shoe covers, caps, and sterile disposable gowns were worn by the patients. 0.5% proparacaine drops were installed, and the eye and its surroundings were cleaned with 10% povidone-iodine. The eye was then covered with a sterile disposable drape and the lids were retracted with a blepharostat device.

The diagnosis of acute endophthalmitis after intravitreal injection was defined as symptoms and clinical findings of sudden vision loss, eye pain, redness, chemosis, iritis, vitritis, and hypopyon within 4 weeks following the injection. In this period, the patients who applied with the above-mentioned symptoms and signs were accepted as acute endophthalmitis and treated accordingly.

RESULTS

The data of 1026 patients, treated with intravitreal bevacizumab for various indications, were retrospectively analyzed. The mean age of patients was 63.5±10 years. Of the patients, 477 (46%) were female and 549 (54%) were male. The total number of injections administered was 4593, of which 3062 were repeat injections. These 4593 injections were administered to 1427 eyes. The distribution of patients according to the indications for intravitreal bevacizumab is shown in Table 1. Among the indications for intravitreal bevacizumab, DRP was the most common (66.7%), followed by AMD (24.3%). The rate of cases with RVO was 9%.

Table 1. Distribution of patients by intravitreal bevacizumab indication

Disease	Number of patients	(%)
Diabetic retinopathy	684	66.7
Age related macular degeneration	249	24.3
Retinal vein occlusion	93	9
Total	1026	100

Of the 4593 intravitreal injections of bevacizumab, only 1 patient developed acute endophthalmitis. Thus, the incidence of acute endophthalmitis after intravitreal injection of bevacizumab was 0.0217% (at 18 months) and 0.014% per year. The infection rate for each eye was 0.07%. The patient who developed acute endophthalmitis after IVB injection, was a 62-year-old male, with a diabetes diagnosis of 12 years duration, who presented with complaints of pain, redness, watering, and sudden vision loss in his left eye one day after the injection. Visual acuity in the affected eye was hand motion. On examination, there was intense conjunctival hyperemia and chemosis, a fibrin reaction in the anterior chamber, and intense condensation in the vitreous of the left eye. B-scan ultrasonography revealed vitreous condensation and diffuse choroidal inflammation findings. The patient had no history of previous eye surgery. The patient was diagnosed with acute endophthalmitis and an emergency pars plana vitrectomy was carried out on the same day. His visual acuity increased to 6/60 at 3 months postoperatively.

DISCUSSION

Bevacizumab inhibits angiogenesis with its anti-VEGF effect in retinal vascular diseases such as DRP, AMD, and RVO. Studies have shown that it has ocular and systemic side effects.[8] Acute endophthalmitis is the most serious of the ocular complications. Acute endophthalmitis can cause sudden vision loss and severe eye pain.[11] Several studies have been conducted in different regions regarding the incidence of acute endophthalmitis after intravitreal injection of bevacizumab.[9,12-16] Our study found the incidence of acute endophthalmitis to be 0.0217%, 0.014% per year, and 0.07% per eye, comparable to other studies.

Ahmed et al.[9] reported the incidence of acute endophthalmitis as 0.0328%, with a rate of 0.018% per year, and a rate of 0.09% per eye after 3051 IVB injections (single-use prefilled sterile syringe) were administered to 1104 eyes of 743 patients with various indications in their prospective study conducted in Lahore, Pakistan. Haider et al.[12] found the incidence of acute endophthalmitis to be 0.19% after single-use prefilled sterile syringe IVB injection in the city of Lahore, which they administered in the office environment and claimed that there was no difference in safety between the administration in the office environment and the operating room environment.

Artunay et al.[13] in their study, they grouped ten patients together for treatment to provide multiple doses from a single vial and they applied 3022 IVB injections to 1822 eyes and reported the incidence of acute endophthalmitis as 0.006%. Karimi et al.[14] reported that post-injection acute endophthalmitis developed in 9 patients in their retrospective study in which they administered

28,085 IVB injections (They applied it to each patient using a separate vial), and reported the incidence as 0.032%. Pradhan et al.[15] in their retrospective study they administered a separate vial to each patient, found the prevalence of acute endophthalmitis to be 0.048% after 4182 IVB injections. Falvarjani et al.[16] in their retrospective study in Iran, found the incidence of acute endophthalmitis to be 0.1% after 5901 IVB injections in 3975 eyes. In the treatment of acute endophthalmitis, early pars plana vitrectomy is important for prognosis.[17] One day after the injection, acute endophthalmitis developed in the left eye of 1 patient and PPV treatment was urgently administered.

In order to reduce the incidence of acute endophthalmitis after IVB injection, it is important for the team performing the application to comply with the conditions of asepsis hygiene prerequisites for patients, as well as the optimal preparation conditions of bevacizumab. In some centers, applications are made by creating multiple doses from a single vial, and there are studies showing that this causes cluster endophthalmitis.[18] Bavinger et al.[19] stated that bevacizumab filled syringes were associated with a lower risk of endophthalmitis as compared to the other multiple doses. In our study, a separate vial was opened for each IVB injection patient. Patient wearing a mask during injection does not reduce the risk of endophthalmitis.[20] In our study, masks were used in all patients who received injections. Like other eye surgeries, applying povidone-iodine to the eye and covering it with a sterile drape during intravitreal injections reduces the risk of endophthalmitis.[21] We applied povidone-iodine to all eyes and used sterile drape.

Limitations of our study were the small number of patients, the fact that the study was carried out as a single-center study, and the coverage of only one region.

CONCLUSION

We found the incidence of acute endophthalmitis after 4593 IVB injections in 1427 eyes of 1026 patients to be very low (0.0217%), which was similar to other studies. In order to reduce the incidence of acute endophthalmitis, which causes severe vision loss, it is of great importance when using IVB for intravitreal injections to prepare bevacizumab suitable for single use and to comply with the rules of asepsis.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of Gaziantep Islamic Science and Technology University Ethics Committee (Date: 07.06.2022, Decision No: 129.17.18).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Garcia J, Hurwitz HI, Sandler AB, et al. Bevacizumab (Avastin®) in cancer treatment: a review of 15 years of clinical experience and future outlook. *Cancer Treat Rev.* 2020;86:102017.
2. Rosen LS, Jacobs IA, Burkes RL. Bevacizumab in colorectal cancer: current role in treatment and the potential of biosimilars. *Target Oncol.* 2017;12(5):599-610.
3. Ruiz-Moreno JM, Montero JA. Intravitreal bevacizumab to treat myopic choroidal neovascularization: 2-year outcome. *Graefes Arch Clin Exp Ophthalmol.* 2010;248(7):937-941.
4. Jyothi S, Chowdhury H, Elagouz M, Sivaprasad S. Intravitreal bevacizumab (Avastin) for age-related macular degeneration: a critical analysis of literature. *Eye (Lond).* 2010;24(5):816-824.
5. Badalà F. The treatment of branch retinal vein occlusion with bevacizumab. *Curr Opin Ophthalmol.* 2008;19(3):234-238.
6. Seo JW, Park IW. Intravitreal bevacizumab for treatment of diabetic macular edema. *Korean J Ophthalmol.* 2009;23(1):17-22.
7. Zayek M, Parker K, Rydzewska M, Rifai A, Bhat R, Eyal F. Bevacizumab for retinopathy of prematurity: 2-year neurodevelopmental follow-up. *Am J Perinatol.* 2021;38(11):1158-1166.
8. Xu Y, Tan CS. Safety and complications of intravitreal injections performed in an Asian population in Singapore. *Int Ophthalmol.* 2017;37(2):325-332.
9. Ahmed N, Rehman HU, Rafique M, Hamza MS, Mirza HA. Incidence of acute endophthalmitis after intravitreal bevacizumab injection at a tertiary care hospital in Lahore. *Cureus.* 2021;13(2):e13185.
10. Bro T, Derebecka M, Jørstad ØK, Grzybowski A. Off-label use of bevacizumab for wet age-related macular degeneration in Europe. *Graefes Arch Clin Exp Ophthalmol.* 2020;258(3):503-511.
11. Durand ML. Endophthalmitis. *Clin Microbiol Infect.* 2013;19(3):227-234.
12. Li T, Sun J, Min J, et al. Safety of receiving anti-vascular endothelial growth factor intravitreal injection in office-based vs operating room settings: a meta-analysis. *JAMA Ophthalmol.* 2021;139(10):1080-1088.
13. Artunay O, Yuzbasioglu E, Rasier R, Sengül A, Bahcecioglu H. Incidence and management of acute endophthalmitis after intravitreal bevacizumab (Avastin) injection. *Eye (Lond).* 2009;23(12):2187-2193.

14. Karimi S, Fakhri N, Ansari I, Hassanpour K, Safi S. Incidence and management of acute endophthalmitis after intravitreal injection of bevacizumab. *Int Ophthalmol.* 2022;42(6):1827-1833.
15. Pradhan E, Duwal S, Bajimaya S, Thapa R, Sharma S, Manandhar A. Acute endophthalmitis after intravitreal bevacizumab injections at the tertiary centre in Nepal. *Nepal J Ophthalmol.* 2018;10(19):107-110.
16. Falavarjani KG, Modarres M, Hashemi M, et al. Incidence of acute endophthalmitis after intravitreal bevacizumab injection in a single clinical center. *Retina.* 2013;33(5):971-974.
17. Khan P, Khan L, Mondal P. Cluster endophthalmitis following multiple intravitreal bevacizumab injections from a single use vial. *Indian J Ophthalmol.* 2016;64(9):694-696.
18. Hébert M, You E, Hammamji K, et al. Impact of patient face mask use on endophthalmitis after intravitreal anti-VEGF injections. *Can J Ophthalmol.* 2022;57(6):364-369.
19. Bavinger JC, Yu Y, VanderBeek BL. Comparative risk of endophthalmitis after intravitreal injection with bevacizumab, aflibercept, and ranibizumab. *Retina*. 2019;39(10):2004-2011.
20. Tanaka K, Shimada H, Mori R, et al. Safety measures for maintaining low endophthalmitis rate after intravitreal anti-vascular endothelial growth factor injection before and during the COVID-19 pandemic. *J Clin Med.* 2022;11(3):876.
21. Sousa DC, Jalil A, Patton N, et al. Early pars plana vitrectomy in acute endophthalmitis: The Manchester Series. *Ophthalmic Surg Lasers Imaging Retina.* 2022;53(2):96-102.