ORIGINAL ARTICLE

Safety Profile of Intravitreal Bevacizumab Injection: A Five Year Retrospective Analysis

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Abstract:

Objective: To evaluate the safety profile of office-based intravitreal Bevacizumab injection.

Methods: This was a retrospective observational study conducted at the private clinic of the author in Dera Ismail Khan, Pakistan from January 2017 to December 2021. The sampling method was non-probability consecutive sampling from the patients receiving intravitreal Bevacizumab (Avastin) injection for various retinal disorders. Each injection was treated as an independent event. Sample size was calculated using Raosoft online calculator keeping margin of error 2% and 95% confidence level. Data analysis was performed using SPSS-20 software

Results: A total of 2377 patients receiving intravitreal Bevacizumab injection were included in the study. Of these, 1201 (50.53%) were female and 1174 (49.47%) were male. Two cases (0.084%; 95% CI: 0.010–0.302%) of post-injection endophthalmitis occurred. Minor complications included subconjunctival hemorrhage (n=7; 0.29%) and conjunctival hyperemia (n=9; 0.38%). No retinal detachments, lens trauma, or sustained intraocular pressure rises were observed.

Conclusion: Intravitreal Bevacizumab injection is a safe procedure when performed with strict aseptic technique. *Al-Shifa Journal of Ophthalmology 2025; 21(4): 234-238. Al-Shifa Trust Eye Hospital, Rawalpindi, Pakistan.*

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Introduction:

Age-related macular degeneration (AMD), diabetic macular edema (DME) and retinal vein occlusion (RVO) are among the common causes of severe visual impairment throughout the world[1]. Neovascular age-related macular degeneration (nAMD) is the leading cause of profound vision loss in high-income countries[2,3]. Intra-vitreal injections of anti-VEGF agents have become the mainstay of treatment for such retinal disorders over the last one and a half decades. Bevacizumab (Avastin) was initially used as off-label drug for the treatment of such retinal diseases in 2005[4]. Soon, there was the emergence of other agents like Pegabtanib, Ranibizumab (Lucentis) and Aflibercept (Eylea)[5,6]. Commonly used treatment protocols of these anti-VEGF injections include fixed monthly injections, pro-re-nata (PRN) and treat-and-extend (TAE)[7,8]. Among these, Bevacizumab is one of the most promising approaches to the management of these retinal disorders[4]. Although these later agents are FDA

approved but Avastin remains the most cost-effective option.

As far as the efficacy of Avastin is concerned, many clinical trials including CATT[4] trial, IVAN[9] study, MANTA[10] trial, LUCAS[11] trial and GEFAL[12] trial have demonstrated that Bevacizumab is non-inferior to Ranibizumab. However, one major issue in the use of Bevacizumab is its non-FDA approval. As Bevacizumab (Avastin) is available in 4 ml vial, so needs to be re-packaged for intra-ocular use which increases the risk of contamination and endophthalmitis. Globally reported endophthalmitis rates range from 0.02% to 0.09%, mostly within hospital or office settings. This study aims to evaluate the safety of office-based intravitreal Bevacizumab injections regarding risk of post-injection endophthalmitis.

Methodology:

This was a retrospective observational study at a private ophthalmology clinic in Dera Ismail Khan from January 2017 to December 2021. Ethical approval was obtained from the Ethical Review Committee (No.1453/HR, dated 11/12/2021). The sampling method was non-probability consecutive sampling from the patients receiving intravitreal Bevacizumab (Avastin) injection for various retinal disorders. Sample size was calculated using Raosoft online calculator, keeping margin of error 2% and 95% confidence level. Patients ≥30 years receiving Bevacizumab for nAMD, DME, PDR, RVO and certain other retinal disorders with both first and repeat injections counted as individual patient. Patients with pre-existing ocular infection, hypersensitivity to Bevacizumab, prior injection-related complications and lack of follow-up within two weeks were excluded from the study.The study author personally prepared and administered all injections. A single puncture of Bevacizumab vials was made under sterile conditions; aliquots were drawn into sterile syringes, stored at 2–8 °C and used within seven days. Injection site (inferior-temporal quadrant) was disinfected with 5% povidone-iodine; the periocular skin was scrubbed with 10% povidone iodine solution. The upper eyelid was retracted and held by the assistant and the lower eyelid by the injecting surgeon and the injection was administered without the use of an eyelid speculum. The protocol ensured that lashes were completely isolated from the injection site to prevent contamination. After the procedure, topical moxifloxacin eye drops were instilled and patients were advised to continue it for five more days. Patients were advised to report pain, redness, or sudden vision loss.

Patients were evaluated on first and second week. The primary safety outcome was the occurrence of post injection endophthalmitis. Endophthalmitis was diagnosed by clinical evaluation (Vision loss, anterior chamber and vitreous cellular reaction) of individual cases. Other complications including sub-conjunctival hemorrhage, damage to crystalline lens, retinal detachment and raised IOP were recorded. Data were analyzed using SPSS version 20. Descriptive statistics of demographic variables were performed by frequency and percentage.

Results:

A total number of 2377 patients (repeated injections counted independently) receiving intravitreal Bevacizumab injection were included in the study. Of these, 1201 (50.52%) were female and 1174 (49.48%) were male. Based on age, patients were divided into three groups; those under < 40 years were 161(6.78%), 40-50 years were 639 (26.88%) and >50 years were 1577(66.34%). During the study period, a total number of 454 patients were treated for nAMD(19.11%), 908 patients for DME (38.20%), 252 for PDR (10.60%), 639 for RVO (26.88%) and 124 others (5.21%), including patients with retinal vasculitis, myopic CNV, neovascular glaucoma and unexplained vitreous hemorrhage. Year wise distribution of gender, age and retinal disorders is shown in Table 1.

Table 1: Year wise frequency distribution of Gender, Age and Retinal disorder

	2017	2018	2019	2020	2021
Gender					
Male	198(60%)	198(45%)	268(54.70%)	225(41.14%)	287(50.36%)
Female	132(40%)	242(55%)	222(45.30%)	322(58.86%)	283(49.64%)
Age group					
<40 years	19(5.75%)	26(5.91%)	47(9.60%)	41(7.50%)	28(4.92%)
40-50 years	84(25.47)	95(21.59%)	114(23.26%)	105(19.20%)	241(42.28%)
>50 years	227(68.79%)	319(72.50%)	401(67.14%)	401(73.30%)	301(52.80%)
Retinal disorders					
nAMD	62(18.80%)	82(18.65%)	102(20.83%)	93(17.02%)	115(20.19%)
DME	148(44.84%)	182(41.36%)	149(30.42%)	191(34.92%)	238(41.76%)
PDR	35(10.61%)	47(10.68%)	51(10.40%)	53(9.68%)	66(11.57%)
RVO	78(23.63%)	115(26.13%)	166(33.87%)	168(30.71%)	112(19.64%)
Others	7(2.12%)	14(3.18%)	22(4.48%)	42(7.67%)	39(6.84%)
Total	330(100%)	440(100%)	490(100%)	547(100%)	570(100%)

During this five-year period only 2 (0.084%; 95% CI: 0.010–0.302%) cases suffered from post-injection endophthalmitis. Minor complications included subconjunctival hemorrhage (n=7; 0.29%) and conjunctival hyperemia (n=9; 0.38%). No retinal detachments, lens trauma, or sustained intraocular pressure rises were observed.

Discussion:

There has been a long debate in the literature on the efficacy and safety of different anti-VEGF agents. A systematic review synthesized the results from 19 RCTs to compare the effectiveness and safety of bevacizumab, ranibizumab and aflibercept and concluded that bevacizumab was as effective as ranibizumab and ranibizumab was as effective as aflibercept[13]. Regarding systemic side effects, Campbell et al showed the intravitreal use of anti-VEGF agents was not associated with significant risk of acute myocardial infarction, ischemic stroke, congestive heart failure and venous thromboembolism[14].

In our study over five years, only 2 (0.084%; 95% CI: 0.010–0.302%) patients suffered from post-injection endophthalmitis. This result is comparable to international data. For instance, the American Society of Retina Specialists

(ASRS) reported administration of 16,115 intravitreal anti-VEGF injections (90% Avastin) with only one case of post-injection endophthalmitis[15]. Vireo-retinal surgeons of Minnesota reported administration of 46,431 injections (56% Avastin) with an endophthalmitis rate of 0.01% for Avastin and 0.02% for Lucentis[15]. An Indian study reported a rate of 0.08% endophthalmitis in a series of 3806 patients[16]. These findings demonstrate a favourable safety profile for intravitreal injection of Avastin (Bevacizumab) when administered under the described protocols.

In our study, DME (38.20%) was the most common indication for Injection Bevacizumab, followed by RVO (26.88%) and then nAMD (19.11%). Similar findings have been reported by Jain P et al in India, where DME (27%) was the most frequent indication for Avastin injection, followed by AMD (26%) and then RVO (12%)[16]. In contrast, Western studies often reported nAMD as the most common indication for intravitreal anti-VEGF injections[17]. The observed endophthalmitis rate of 0.084% aligns with previously reported international data ranging from 0.02% to 0.09%[18,19].

Contributing factors likely include strict aseptic measures, single-puncture aliquoting, & surgeon-administered injections. Use of manual lid retraction, though differing from some guidelines, did not result in increased infection rates and may be acceptable when handled carefully.

Conclusions:

The endophthalmitis rate observed in this study is consistent with international benchmarks. The low complication rate may be attributed to strict aseptic protocols, surgeon-prepared syringes and structured post-injection monitoring. These findings support the safety of intravitreal Bevacizumab administration.

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