Incidence of endophthalmitis after intravitreal injections at a tertiary care hospital

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ABSTRACT • RÉSUMÉ

Objective: To report the incidence of endophthalmitis after the use of intravitreal injection for anti–vascular endothelial growth factor therapy.

Methods: This was a single-centre retrospective study conducted at the Aga Khan University Hospital, Pakistan. A total of 11 128 injections were administered to 2054 patients between January 2013 and December 2015. All procedures were performed in an operating room setting, and postinjection antibiotics were prescribed.

Results: Three cases of endophthalmitis occurred during the study period, with the per-injection risk of endophthalmitis being 0.027%.

Conclusion: The results highlight the benefit of administering intravitreal injections in a surgical setting in addition to enforcing quality protocols. We also recommend further investigation to scrutinize the role of antibiotics prescribed after deploying intravitreal injections so that unnecessary use of such may be curtailed.

Objet : Quantifier l'incidence d'endophtalmie secondaire à l'injection intravitréenne d'un médicament anti-FCEV (facteur de croissance endothélial vasculaire).

Méthodes : Il s'agissait d'une étude rétrospective réalisée dans un seul centre, soit l'Aga Khan University Hospital, au Pakistan. Au total, 11 128 injections ont été administrées à 2054 patients entre janvier 2013 et décembre 2015. Toutes les injections ont eu lieu au bloc opératoire, et les patients ont reçu une antibiothérapie après l'injection.

Résultats : Il s'est produit 3 cas d'endophtalmie pendant la période d'étude, ce qui se traduit par un risque d'endophtalmie de 0,027 % par injection.

Conclusion : Ces résultats soulignent l'intérêt d'administrer les injections intravitréennes au bloc opératoire tout en respectant les protocoles d'assurance de la qualité. Nous recommandons également d'examiner plus à fond le rôle des antibiotiques post-injection, de façon à éviter l'administration inutile de ces médicaments.

Vascular endothelial growth factor (VEGF), a proangiogenic cytokine, is central to both physiologic and pathologic angiogenesis. Overexpression of VEGF in response to hypoxia leads to endothelial cell stimulation and is hypothesized to be causative in the pathophysiology of various ocular diseases, including diabetic retinopathy (DR), neovascular age-related macular degeneration, and retinal vein occlusion. The resulting vascular fragility is a significant cause of visual loss secondary to edema, hemorrhage, and/or fibrovascular proliferation causing retinal detachment.[1,2]

Introduction of anti-VEGF therapy has revolutionized the approach to these retinal diseases. Pegaptanib (Macugen) was the first to be approved and was soon followed by other agents, including ranibizumab (Lucentis; Genentech, San Francisco, Calif.), bevacizumab (Avastin; Genentech), and aflibercept (Eylea; Regeneron, Tarrytown, N.Y.).[3] The older therapeutic modalities for managing neovascularization included laser photocoagulation and photodynamic therapy. However, these were destructive and nonphysiological. In comparison, anti-VEGF exerts its influence by potent inhibition of increased levels of VEGF. Treatment with anti-VEGF has become a standard of care and is used in clinical practice worldwide to manage and stabilize angiogenic retinal diseases. In the United States, the number of injections performed has increased exponentially, from 4215 injections in 2001 to 2.5 million injections in 2011. Similar increases have been noted in Canada and the United Kingdom.[4] Ranibizumab and aflibercept have also been FDA-approved, whereas bevacizumab is being used off-label for this indication with increasing frequency.[2,3,5–7]

Local complications can occur after anti-VEGF therapy, including injection-related intraocular inflammation, rhegmatogenous retinal detachment, ocular hemorrhage, and intraocular pressure elevation. The most dreaded complication is infectious endophthalmitis (EO), a potentially sight-threatening pathology. In multicentre clinical trials, incidence of EO per patient has been reported to range from 0.019% to 1.6%. Multiple large-scale meta-analyses have put incidence rates at relatively lower figures. McCannel[8] found a rate of 52 from 105 536 injections (0.049%; 1 in 2030), Fileta et al.[9] calculated a rate of 197/350 535 (0.056%; 1 in 1779), and more recently,

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Merani and Hunyor[4] reported an incidence rate of 144 of 510 396 (0.028%; 1/3544).

There is paucity of data from South Asia regarding incidence of EO after intravitreal injection (IVI) administration and whether it compares favourably with globally reported incidence. Our study therefore aims to report EO rates in our setting. Clinical presentation, treatment, and outcomes will also be discussed.

Patients and Methods

This single-centre, retrospective study was conducted at the Aga Khan University Hospital, Pakistan, from December 2015 to May 2016. The hospital's ethics review committee approved the study. All patients who received intravitreal anti-VEGF therapy between January 1, 2013, and December 31, 2015, were included. They were identified using the hospital's billing records system. Collected information included patient demographics, type of injection administered, and indication. Written informed consent was obtained before all IVIs were performed.

Cases of established or presumed EO were similarly discerned through an identical registry and billing system. Records of these patients were further reviewed for details on etiology, clinical progress, and treatment outcomes. Presumed EO was defined as any degree of intraocular inflammation requiring intravitreal antibiotics. Proven EO was based on positive gram stain or culture. Patients who did not meet the criterion for the diagnosis of EO or who developed EO secondary to another etiology were excluded.

All IVIs in our setting were performed in designated surgical day care operating rooms (ORs) using a standardized protocol. Injections were administered with a 29-gauge needle in the infratemporal quadrant at a distance of 3.5–4.0 mm away from the limbus. Topical 0.5% proparacaine and 4% lidocaine were used for conjunctival anaesthesia. Eyelids, eyelashes, and conjunctiva were prepared using 5% povidone-iodine solution. A fenestrated self-adhesive surgical drape that covered the patient's nose and mouth and a sterile lid speculum were used. Injections were administered by 6 different ophthalmologists or the chief resident under supervision. Surgical hand sepsis (povidone-iodine) and change of sterile gloves was performed before every new patient was treated. Use of face masks was uniformly practised by all medical personnel, and all conversation paused at the time of administration. Use of preinjection antibiotics was not practised at our institute. Type and duration of postinjection antibiotics were determined at the discretion of the individual treating physicians.

Initial management was determined by each individual evaluating ophthalmologist. Aqueous or vitreous fluid was sent for microbial culture in all cases and empiric treatment initiated. Culture results were reviewed and treatment changed accordingly, if needed.

Descriptive analysis was carried out for discrete and continuous variables, and the results are presented in the form of percentages and/or means. Main outcome measures were cases of presumed or proven EO. SPSS version 19 was used for data analysis.

Results

A total of 11 128 IVIs were administered to 2054 patients over the 3-year study interval. Bevacizumab was given to 65% (n = 1335) patients, ranibizumab to 34% (n = 698), and aflibercept to 1% (n = 21). DR defined either as proliferative retinopathy or diabetic maculopathy (DR, n = 1078; 52.5%) was the most common indication. Other indications included macular degeneration (ge-related macular degeneration, n = 647; 31.5%), choroidal neovascular membrane (n = 64; 3.09%), and venous occlusions (n = 89; 4.32%). Cystoid macular edema and central serous retinopathy accounted for 4.9% and 2.5% of indications. Less-frequent pathologies such as retinopathy of prematurity comprised the remaining (1.2%) indications.

Per-injection risk of presumed EO was 3 of 11 128 (0.027%), and culture-proven incidence was 0.0089% (1/11 128). Per-patient EO rates were 0.07%, 0.14%, and 4.76% with bevacizumab, ranibizumab, and aflibercept, respectively. Cumulative per-patient risk was 0.15%.

Case 1

A 36-year-old male who was receiving intravitreal anti-VEGF therapy in his left eye for cystoid macular edema presented with blurred vision 2 days after his sixth dose of anti-VEGF. His visual acuity (VA) had dropped from 20/25 to 20/400, and he was noted to have anterior chamber cells, keratic precipitates, and vitreous inflammation. He was treated with intravitreal antibiotics and dexamethasone injection, in addition to topical antibiotics and oral Augmentin. At 3-month follow-up, the VA improved to baseline 20/25.

Case 2

A 55-year-old hypertensive male with diabetes receiving anti-VEGF therapy for DR reported left ocular pain and visual loss 2 days after his first bilateral aflibercept administration. Before this, his VA was 20/30. Conjunctival congestion, hypopyon, and disorganized anterior chamber cells were seen on examination. A diagnosis of left ocular EO was made. On further visits, optic disc was not appreciated, and VA had dropped to hand movements. B-scan showed inferior retinal detachment. He was treated with vitrectomy and intravitreal and oral antibiotics. Group D streptococcus was isolated on culture. At 4-month follow-up, VA was 20/400.