

VISION ACADEMY VIEWPOINT

The Vision Academy is a partnership between Bayer and ophthalmic specialists, established with the aim of addressing key clinical challenges in the field of retinal diseases: www.visionacademy.org.

Use of Topical Antibiotics with Intravitreal Injections

Background

Intravitreal injections are increasing in frequency due to the widespread adoption of anti-vascular endothelial growth factor (VEGF) therapies for the management of retinal diseases. Many physicians continue to use topical antibiotics alongside intravitreal injections with the expectation of minimizing the risk of serious complications such as endophthalmitis, yet evidence is lacking regarding the efficacy of topical antibiotics in preventing endophthalmitis following intravitreal injection.

A review of the literature and available evidence was conducted to:

- Determine the validity of the use of topical antibiotics as a prophylactic measure alongside intravitreal anti-VEGF injections
- Evaluate the potential effect of topical antibiotics on the prevention or reduction of intravitreal injection-associated infections

Endorsed by the Vision Academy
in May 2019.

 Full consensus  Variations in opinion

Viewpoint

An aseptic technique for intravitreal injection is essential for minimizing the risk of serious complications such as endophthalmitis. Procedures should ensure adequate anesthesia and asepsis, including a topical broad-spectrum microbicide (such as povidone-iodine), and should be conducted according to prescribing information, medical standards, and applicable guidelines.

Based on an extensive literature search, the Vision Academy does not recommend the use of topical antibiotics alongside intravitreal injections for the following reasons:

- There is **no evidence** for prevention of infection and they may even be associated with an increased risk of endophthalmitis¹⁻⁴
- There is **no evidence** for the reduction of infection-related morbidity¹
- Repeated use is **proven to increase** the occurrence of antibiotic resistance and potentially increased virulence¹
- There is **additional cost and burden** to patients, physicians, and healthcare systems¹

Following intravitreal injection, patients should be instructed to report any symptoms suggestive of endophthalmitis (e.g. eye pain, redness of the eye, photophobia, and blurring of vision) without delay.

Further considerations

Topical antibiotic use **prior to** the injection procedure has an appealing rationale, since the entry of organisms into the vitreous typically occurs at the time of injection; however, there have been no prospective studies demonstrating that pre-injection antibiotics reduce the risk of endophthalmitis and the available literature indicate the omission of prophylactic application can be justified.^{1,5-8}

In addition, application of topical antibiotics, either **concurrent with** or **after** the injection procedure, has not shown additional benefit over topical broad-spectrum microbicides and antiseptic administration.^{9,10}



References

1. Merani R and Hunyor AP. Endophthalmitis following intravitreal anti-vascular endothelial growth factor (VEGF) injection: A comprehensive review. *Int J Retina Vitreous* 2015; 1: 9.
2. Menchini F, Toneatto G, Miele A *et al*. Antibiotic prophylaxis for preventing endophthalmitis after intravitreal injection: a systematic review. *Eye (Lond)* 2018; 32 (9): 1423–1431.
3. Reibaldi M, Pulvirenti A, Avitabile T *et al*. Pooled estimates of incidence of endophthalmitis after intravitreal injection of anti-vascular endothelial growth factor agents with and without topical antibiotic prophylaxis. *Retina* 2018; 38 (1): 1–11.
4. Bande MF, Mansilla R, Pata MP *et al*. Intravitreal injections of anti-VEGF agents and antibiotic prophylaxis for endophthalmitis: A systematic review and meta-analysis. *Coi Rep* 2017; 7 (1): 18088.
5. Lau PET, Jenkins KS and Layton CJ. Current evidence for the prevention of endophthalmitis in anti-VEGF intravitreal injections. *J Ophthalmol* 2018; 2018: 8567912.
6. Yannuzzi NA, Gregori NZ, Rosenfeld PJ *et al*. Endophthalmitis associated with intravitreal injections of anti-VEGF agents at a tertiary referral center: in-house and referred cases. *Ophthalmic Surg Lasers Imaging Retina* 2018; 49 (5): 313–319.
7. Zafar S, Hamid A, Bin Mahmood SU *et al*. Incidence of endophthalmitis after intravitreal injections at a tertiary care hospital. *Can J Ophthalmol* 2018; 53 (2): 94–97.
8. Stem MS, Rao P, Lee IJ *et al*. Predictors of endophthalmitis after intravitreal injection: a multivariable analysis based on injection protocol and povidone iodine strength. *Ophthalmol Retina* 2019; 3 (1): 3–7.
9. Li AL, Wykoff CC, Wang R *et al*. Endophthalmitis after intravitreal injection: role of prophylactic topical ophthalmic antibiotics. *Retina* 2016; 36 (7): 1349–1356.
10. Storey P, Dollin M, Pitcher J *et al*. The role of topical antibiotic prophylaxis to prevent endophthalmitis after intravitreal injection. *Ophthalmology* 2014; 121 (1): 283–289.
11. Yin VT, Weisbrod DJ, Eng KT *et al*. Antibiotic resistance of ocular surface flora with repeated use of a topical antibiotic after intravitreal injection. *JAMA Ophthalmol* 2013; 131 (4): 456–461.
12. Milder E, Vander J, Shah C *et al*. Changes in antibiotic resistance patterns of conjunctival flora due to repeated use of topical antibiotics after intravitreal injection. *Ophthalmology* 2012; 119 (7): 1420–1424.
13. Radhika M, Mithal K, Bawdekar A *et al*. Pharmacokinetics of intravitreal antibiotics in endophthalmitis. *J Ophthalmic Inflamm Infect* 2014; 4: 22.
14. American Society of Retina Specialists. ASRS Global Trends in Retina. Available at: https://www.asrs.org/content/documents/2014_global_trends_comprehensivepostmtg.pdf. Accessed February 2019.

Antibiotic resistance is a serious concern. In multiple large case series comparing intravitreal injection with or without the use of antibiotics, there is a numerical trend in most toward increased rates of endophthalmitis.^{1,10} Moreover, the repetitive nature of intraocular injection of anti-VEGF agents, and thus repeated use of topical antibiotics, significantly increases the potential for colonization of the ocular surface with resistant bacteria.^{11,12} This approach also interferes with clinical care models and increases cost and patient inconvenience, particularly when patients are managed in a reactive/*pro re nata* (as needed) manner. Furthermore, topical antibiotics have poor penetration into the eye due to various physiological barriers, so they do not reach therapeutic levels in the vitreous.¹³



There are significant regional differences concerning the use of topical antibiotics in intravitreal injection clinics. In 2014, 84% of physicians from the Asia-Pacific region said they used topical antibiotics, compared with only 11% of US physicians.¹⁴ Reasons for continued use include personal preference, peer-pressure, and medico-legal concerns. In Japan, the use of topical antibiotics alongside anti-VEGF injections is mandated by the label and considered standard use. Therefore, changes in practice habits may be achieved through the revision of drug labels and the amendment of local and professional society guidelines.



Full consensus



Variations in opinion