Commentary: Usage of intravitreal steroids in endophthalmitis: Horns of a dilemma

The usage of steroids intravitreally along with antimicrobials for endophthalmitis management has been marred with controversy for decades. To a large extent, management of endophthalmitis has been based on physician discretion and has a lot of variability between cases. The rationale behind steroids/anti-inflammatory agents is that endophthalmitis leads to severe inflammation and bystander damage to intraocular tissues, especially the neurosensory retina, resulting in irreversible functional changes. Suppressing this inflammation may help reduce the irreversible damage and shorten the overall disease course. It is not well understood whether the damage to the visual function is due to the infectious agent or the immune response developed by the host in response to it.

There is no unanimous understanding regarding whether steroids have any definite role in visual improvement as demonstrated by this meta-analysis, and previous reports as well.[1] The current article evaluated studies dealing with bacterial endophthalmitis alone. Considering fungal endophthalmitis, there is even lesser amount of evidence regarding the status of steroids, as steroids are believed to flare up intraocular pathogens. One way to approach this conundrum is to consider steroids once an initial dose of intravitreal antimicrobials has been given and/or vitrectomy has been done to reduce the microbial load. Then, if the patient is undergoing further intravitreal injections, intravitreal steroids can be considered.

However, steroids may have a definite role in preserving the anatomical integrity during initial endophthalmitis management, preventing outcomes such as phthisis bulbi or requirement of evisceration.[2] The inconsistencies in management rationale, type of outcomes reported, and follow-up protocols in previous studies make a uniform consensus difficult—more so because quantifying resolution or a successful management of endophthalmitis is not standardized. Steroids may reduce tissue inflammation in the initial period, which in turn can reduce the chances of eyes requiring further vitrectomies or IOL explantation procedures.

Another point to ponder is that the older evidence of intravitreal steroids is from days when an initial intravitreal regimen of antibiotics with or without steroids with additional injections would be considered followed by a period of observation. A decision of vitrectomy would be taken after noting the resolution pattern and based on physician discretion. However, with complete and early vitrectomy, as is becoming the norm gradually, after the organism load has been reduced, intravitreal steroids may also be considered in the retreatment regimens.[3] The biggest gray zone is for cases of fungal endophthalmitis, where no clear evidence is available due to extreme variability in clinical presentations. Authors have noted that visual outcomes may be better in fungal endophthalmitis with the usage of systemic or topical steroids under a cover of antifungal therapy.[4] However, the sensitivity of the fungi to the antifungal agent and the timing and dosage of steroids must be considered before starting the same.

Currently, although we have an armamentarium of drugs and surgical modalities, the outcomes of endophthalmitis remain poor because of unknown host and organism related factors, which cannot be treated using conventional methods. Experimental studies in animals have shown that infectious endophthalmitis can induce the expression of cytokines, chemokines, and apoptotic factors. Recently, authors have also studied inflammatory changes in the vitreous taken from endophthalmitis patients and tried to identify factors that can predict the clinical outcomes of the disease.[5][6] Apoptotic proteins such as Bax and Fas expression peaks at 48 h after initial endophthalmitis onset, and apoptotic rate peaks at 72 h under experimental conditions.[9]

Many such host innate immune pathways are under research to try and target for endophthalmitis management in addition to antimicrobials. Reducing the concentrations of individual inflammatory mediators might limit the bystander damage to tissues while allowing a more favorable wound healing response.
along with neuroprotection. A TLR2 agonist, Pam3Cys, has been explored as a molecule which attenuates clinical inflammation, reduces bacterial load in retina, and preserves retinal architecture with electroretinogram in mice retina. Anti-TNFα therapy may also have role in improving endophthalmitis outcomes. Other possible drug targets in stage of development are anti IL6, anti IL1beta, anti IL8, etc. Scientists have also employed macrophage membrane-coated nanosponges as decoys to bind excess cytokines and chemokines in the vitreous to prevent cytotoxicity. Further studies are needed to identify molecules that can help in reducing inflammation in severe and fulminating endophthalmitis cases and salvage such eyes toward both optimum anatomical and functional outcomes.

**Sagnik Sen, Naresh Babu Kannan**  
Department of Retina and Vitreous Services, Aravind Eye Hospital, Madurai, Tamil Nadu, India  
**Correspondence to:** Dr. Sagnik Sen, Department of Retina and Vitreous Services, Aravind Eye Hospital, Madurai, Tamil Nadu, India.  
E-mail: riksag@gmail.com

**References**

1. Soekamto C, Rosignoli L, Zhu C, Johnson DA, Sohn JH, Bahadorani S. Visual outcomes of acute bacterial endophthalmitis treated with adjuvant intravitreal dexamethasone: A meta-analysis and systematic review. Indian J Ophthalmol 2022;70:2835-41.

2. Das T, Jalali S, Gothwal VK, Sharma S, Naduvilath TJ. Intravitreal dexamethasone in exogenous bacterial endophthalmitis: Results of a prospective randomised study. Br J Ophthalmol 1999;83:1050-5.

3. Dib B, Morris RE, Oltmanns MH, Sapp MR, Glover JP, Kuhn F. Complete and early vitrectomy for endophthalmitis after cataract surgery: An alternative treatment paradigm. Clin Ophthalmol 2020;14:1945-54.

4. Majji AB, Jalali S, Das T, Gopinathan U. Role of intravitreal dexamethasone in exogenous fungal endophthalmitis. Eye (Lond) 1999;13:660-5.

5. Sauer A, Candolfi E, Gaucher D, Creuzot-Garcher C, Bron A, Chiquet C, et al. Intraocular cytokine levels in post-cataract endophthalmitis and their association with visual outcome. Ocul Immunol Inflamm 2018;26:964-70.

6. Hao X, Yi C, Wang Y, Li J, Huang F, He L, et al. Identification of intraocular inflammatory mediators in patients with endophthalmitis. Mol Vis 2016;22:563-74.

7. Escario P, Commodaro AG, Arantes T, de Castro CMMB, Diniz Mde FA, Brandt CT. Analysis of Cyto- kines in presumed acute infectious endophthalmitis following cataract extraction. J Clin Exp Ophthalmol 2014;5:335.

8. Deshmukh D, Chakrabarti M, Jayasudha R, Hasnat Ali M, Tyagi M, Sharma S, et al. Elevated cytokine levels in vitreous as biomarkers of disease severity in infectious endophthalmitis. PLoS One 2018;13:e0205292. doi: 10.1371/journal.pone.0205292.

9. Pharmacakis NM, Petropoulos IK, Georgakopoulos CD, Vantzou CV, Anastassiou ED, Mavropoulos A, et al. Apoptotic mechanisms within the retina in Staphylococcus epidermidis experimental endophthalmitis. Graefes Arch Clin Exp Ophthalmol 2009;247:667-74.

10. Talreja D, Singh PK, Kumar A. In vivo role of TLR2 and myD88 signaling in eliciting innate immune responses in staphylococcal endophthalmitis. Invest Ophthalmol Vis Sci 2015;56:1719-32.

11. Ramadan RT, Moyer AL, Callegan MC. A role for tumor necrosis factor-alpha in experimental Bacillus cereus endophthalmitis pathogenesis. Invest Ophthalmol Vis Sci 2008;49:4482–9.

12. LaGrow AL, Coburn PS, Miller FC, Land C, Parkunan SM, Luk BT, et al. A novel biomimetic nanosponge protects the retina from the enterococcus faecalis cytolsin. mSphere 2017;2:e00335–17. doi: 10.1128/mSphere.00335-17.

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.