Commentary: Is it time to re-evaluate the empiric intravitreal antibiotic therapy in infectious bacterial endophthalmitis?

Intravitreal antibiotics and vitrectomy in selected instances have been the standard of care since the mid-1990s following the Endophthalmitis Vitrectomy Study (EVS) recommendations.[1] The EVS suggestion for presenting vision-guided core vitrectomy has been challenged in the following decades.[2] It is related to the advancements in vitrectomy technology and techniques, including small-gauge instrumentations, faster cutting rates, superior fluidics, and wide-angle visualization. Early and complete vitrectomy has been recommended by several authors and/or is currently practiced in several countries. The EVS recommendation of two intravitreal antibiotics in post-cataract surgery acute endophthalmitis has stood the test of time. Currently, intravitreal therapy with antibiotics and antifungal agents is the primary treatment modality in bacterial and fungal endophthalmitis, respectively, and is no longer confined to post-cataract surgery infection.

The use of intravitreal antibiotics in infectious endophthalmitis follows the pioneering work of Peyman *et al.* in the 1970s.[3] While they recommended an antibiotic–corticosteroid combination (gentamicin + dexamethasone) intravitreal injection, the EVS included two antibiotics (amikacin and vancomycin) and excluded dexamethasone in the intravitreal drug regimen. The rationale of two antibiotics is for adequate antibiotic coverage of gram-positive (vancomycin) and gram-negative (amikacin) infections.[1] However, in the final EVS recommendation, ceftazidime replaced amikacin to avoid aminoglycoside, including amikacin, -induced macular infarction.[4] In the EVS, the susceptibility of vancomycin and ceftazidime was 100% and 89.5% to gram-positive and gram-negative bacteria, respectively.[5] In the late 1990s, we reported a reduced susceptibility of these antibiotics – vancomycin 84% against gram-positive and ceftazidime 61% against gram-negative bacterial isolates in infectious endophthalmitis in India.[6] Subsequently, we also reported ceftazidime and amikacin-resistant gram-negative bacterial infection.[7,8] In a larger analysis of 3319 consecutive culture-positive infectious endophthalmitis spread over a quarter of a century (1991–2015; 85.6% bacterial endophthalmitis and 67.7% gram-positive bacterial endophthalmitis), 96% of gram-positive organisms were susceptible to vancomycin and up to 79% gram-negative organisms were susceptible to fluoroquinolones. Additionally, our study documented an increased resistance to ceftazidime, from 31% in 2005 to 62% in 2015.[9] This knowledge is crucial, given India's higher incidence of gram-negative bacterial endophthalmitis.[10]

While vancomycin has retained an excellent susceptibility against gram-positive microorganisms, several other antibiotics have been used to overcome the resistant gram-negative bacteria. These include colistin, imipenem, and piperacillin–tazobactam. In this issue of the journal, there is a report of a prospective study comparing a different combination of intravitreal antibiotic – ceftazidime, imipenem, and piperacillin–tazobactam – with vancomycin in the treatment of infectious endophthalmitis. Based on the vitreous drug assay, the authors did not find the superiority of other antibiotic combinations over the currently used vancomycin–ceftazidime combination.[11] But this conclusion suffers from strong scientific validity because of inadequate sample size, imperfect randomization, and fewer instances of vitreous drug assay of antibiotics other than vancomycin and ceftazidime.

Irrespective of this conclusion, there is no denying of the emergence of resistant gram-negative bacteria. The selection of the right combination of intravitreal antibiotics in infectious bacterial endophthalmitis should be ideally studied in a large randomized clinical trial (RCT) or decided from big data analysis. RCTs in endophthalmitis are time consuming and cost intensive. Such a study, however, is currently underway in India.[12] The results could be fascinating. Meanwhile, one could continue with the intravitreal vancomycin–ceftazidime antibiotics combination and change to culture susceptibility-adjusted antibiotic when required.

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Access this article online

Quick Response Code:

Website: www.ijo.in

DOI: 10.4103/ijo.IJO_393_22

Cite this article as: Das T. Commentary: Is it time to re-evaluate the empiric intravitreal antibiotic therapy in infectious bacterial endophthalmitis? Indian J Ophthalmol 2022;70:1701-2.