THE ROYAL COLLEGE OF OPHTHALMOLOGISTS

Focus

Summer 2014

An occasional update commissioned by the College.
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Recent advances in Endophthalmitis Management

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Endophthalmitis remains a topic of great importance to the practising ophthalmic surgeon. Advances in both prevention and management are leading to reduced infection rates and better outcomes of infection. Povidone iodine 5% to the ocular surface and 5-10% to the periocular skin, applied for a minimum of 3 minutes, has become the standard of care. The ESCRS document 'Guidelines for prevention and treatment of endophthalmitis following cataract surgery' (2013) discusses in detail the value of intracameral antibiotics at the end of cataract surgery, and also presents evidence pertaining to wound construction, the use of foldable IOLs, choice of IOL material and coatings, and the contribution of surgical complications to the risk of endophthalmitis. Some units, including ours, have also demonstrated reducing endophthalmitis rates after the introduction of mandatory suturing of the corneal incision at the end of cataract surgery, although this remains controversial. Whilst prevention of endophthalmitis remains the overriding surgical concern, the main focus of this article will be the recent advances in the management of suspected endophthalmitis from all causes.

Longitudinal studies of endophthalmitis are beginning to demonstrate evolving trends in both pathogens and antibiotic sensitivities.1 With the increasing uptake of intracameral prophylaxis, shifts in the preponderance of endophthalmitis isolates are emerging. A large Swedish series2 reported a relative increase in rates of enterococcal infections. This, combined with an increase in resistant organisms, may require a future departure from the 'standard' clinical management of acute endophthalmitis.

Exogenous endophthalmitis is a post-surgical or post-traumatic condition, typically presenting within 2-3 days of the original insult. The risk of endophthalmitis after open globe injury is up to 16.5%, but there is evidence this figure is decreasing due to earlier wound closure with antibiotic therapy.3 The epidemiological profile of endogenous endophthalmitis, however, has changed in recent years. There has been a dramatic reduction in AIDS-related cases following the introduction of HAART, and now the majority of cases arise from metastatic spread of infection in patients who are immunocompromised by conditions such as leukaemia. These are patients who are at particular risk of missed diagnosis, and therefore a low threshold of suspicion should be maintained in patients presenting with a vitritis or panuveitis who are immunocompromised (e.g. organ transplantation), who have major illnesses (admission to ITU, malignancy, diabetes), who are intravenous drug users, who have had recent major surgery (e.g. bowel surgery), or in whom sepsis is known or suspected. In cases where a cellular infiltrate requires differentiation between infection and malignancy, a full vitrectomy is recommended, as this yields a superior cellular sample.

The diagnosis of intraocular infection typically involves immediate staining and microscopy of aqueous and vitreous samples for identification of bacterial or fungal pathogens. This is followed by sample culture which may provide identification and sensitivities of the organism to guide further treatment. However, various factors limit the sensitivity of culture techniques, and adjunctive PCR techniques have increasingly been used to improve the diagnostic yield. Conventional PCR detects and amplifies minute amounts of microbial DNA by the use of broad range primers which target eubacterial 16S rDNA or fungal 18S rDNA. More recently, quantitative real-time PCR techniques have been introduced which can expedite and refine the identification process, reduce the risk of contamination and quantify the microbial load.4

Intravitreal drugs used in the treatment of suspected endophthalmitis usually include vancomycin 2mg/0.1ml to

cover gram-positive organisms, and a cephalosporin such as ceftazidime 2mg/0.1ml or an aminoglycoside such as amikacin 0.4mg/0.1ml (in patients allergic to penicillin) to cover gram-negative rods. The high microbial susceptibility rates, combined with an excellent safety profile, support the continued use of these agents.1 Some studies have found ciprofloxacin, a second-generation fluoroquinolone, to have greater efficacy than ceftazidime in treating both gram-positive and gram-negative organisms. However this is thought to reflect discrepancies in local microbiological susceptibility patterns.

For suspected fungal infection, newer generation triazoles (e.g. voriconazole, posaconazole) have good intravitreal penetration when given systemically; Voriconazole appears to have low retinal toxicity when given intravitreally. A new class of drug, the echinocandins (e.g. caspofungin), are active against Candida and Aspergillus, and appear to have fewer adverse events than amphotericin B; however their penetration into the vitreous cavity is poor. As a general rule, pars plana vitrectomy is reserved for moderate to severe vitreous involvement, with adjunctive intravitreal amphotericin B (now available as a liposomal preparation).

Resistance to antimicrobial agents is an issue of increasing importance, particularly as there is evidence of a potential trade-off between the desire to prevent endophthalmitis and the ability to treat it effectively. The ESCRS study did not show any clear benefit to the use of pre- or postoperative topical antibiotics, and the 2013 guidelines state both that bacterial resistance may be induced, and that complete bacterial eradication on the ocular surface is not achieved in any case. The efficacy of prophylactic topical third- and fourth-generation fluoroquinolones such as moxifloxacin and gatifloxacin have been evaluated, but there appears to be increasing resistance of bacteria to these agents, as well as to methicillin/oxacillin. Whilst intracameral cefuroxime is the ESCRS drug of choice for endophthalmitis prophylaxis, it lacks activity against methicillin-resistant Staph. aureus and epidermis (MRSA and MRSE), and with increasing rates of these isolates in endophthalmitis, cefuroxime may become less effective in the future. The RCOphth cataract surgery guidelines (2010) allow for the continuing use of other agents (such as Vancomycin) in units whose endophthalmitis rates have historically remained low, but since Vancomycin is the current drug of choice for treatment of MRSA / MRSE infection, the ESCRS guidelines discourage its use as prophylaxis. Intracameral moxifloxacin is more popular in the US, but there is concern that the widespread use of this fourth-generation quinolone as a prophylactic antibiotic may also promote resistance.

The introduction of the newer fluoroquinolones into the antimicrobial armamentarium have provided an opportunity for adjunctive systemic therapy to be modified. The Endophthalmitis Vitrectomy Study (EVS) concluded that intravenous amikacin and ceftazidime made no difference to the final visual acuity. However, these drugs are known to have poor ocular penetration compared with the fluoroquinolones, so in many units oral Ciprofloxacin 750mg bd po for 10 days has been used as an adjunct. A more recent study has suggested a clinical superiority of oral Moxifloxacin 400mg od po for 10 days over Ciprofloxacin, with quicker resolution of hypopyon, reduced need for repeat intravitreal injection and better chance of a good clinical outcome, even when adjusting for resistance to Ciprofloxacin (rates of which were found to increase over the course of the study).5 However, quinolones are excreted in sweat, and have been found to increase colonisation with MRSA, so in some units the use of these drugs is discouraged.

There remains a weak evidence base for the use of steroid when managing endophthalmitis. Some studies suggest poorer outcomes if steroids are given at the same time as intravitreal antibiotics, whereas others recommend the use of intravitreal 4mg/0.1ml unpreserved Dexamethasone. If not contraindicated by patient factors or suspected fungal infection, oral steroid 1mg/kg od po, commenced 24 hours after intravitreal antibiotics, may also be helpful.

Vitrectomy plays an important role in the management of endophthalmitis, both diagnostically and therapeutically. Although there is no good evidence of the diagnostic superiority of vitrectomy samples over a vitreous tap, there are certain groups that do better therapeutically with early vitrectomy. The EVS found that visual outcomes with vitrectomy and vitreous tap were equivalent except in eyes with PL or worse, and in diabetic patients. A full pars plana vitrectomy is appropriate in cases of vitritis where the diagnosis is uncertain, in moderate to severe fungal infection, and in bacterial endophthalmitis which is non-responsive to two doses of intravitreal antibiotics given over 48 hours. Special situations such as indolent infection with pseudomonas acnes may require capsulectomy.

In summary, there are many developments in the management of endophthalmitis which may merit review of current departmental protocols. Clinicians should be aware of the evolving spectrum of pathogens and antibiotic susceptibilities, and tailor the management of all patients accordingly.

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