18

**Symposium Report**

**XXIV Congress of the ESCRs, London 2006**

**Endophthalmitis following cataract surgery, do we have the answers?**

In our experience in Europe and Scandinavia, MRSA is present in the hospitals but not in the community to a sufficient degree that patients coming from the community for day case surgery are colonised with MRSA and infection would occur.

_**David Seal MD**_

**Surgical theatre hygiene important**

Improvements in surgical technique and instrumentation have largely eliminated Gram-negative bacteria as a cause for endophthalmitis following cataract surgery. However, surgeons should take precautions to avoid other types of contamination, he advised.

For example, HEPA filters should be used to reduce the presence of mycelial spores, and staff members with active eczema should not enter the operating theatre, as they can be prolific shedders of staphylococci.

In addition, absolute care should be taken to ensure that all surgical instrumentation, irrigation fluids and IOls are completely sterilised, Dr Seal said. Moreover, single use eye drops are also preferable to the multiple use variety. A recent study showed that 40 per cent of multiple use eye drops are contaminated with staphylococci, he pointed out.

**Current practices reduce but do not eliminate contamination**

Current prophylaxis procedures generally involve the topical application of povidone iodine or aqueous chlorhexidine. In some centres topical antibiotics are also part of the prophylactic regimen. However, while these measures may reduce the bacterial load by 90-99 per cent, they do not sterilise the eye, Dr Seal noted.

Studies conducted in the early 1990s indicated that at that time bacteria could be isolated from the anterior chamber of 29-43 per cent eyes following cataract surgery using phaco or ECCE. A more recent paper (Parmar et al., American Journal of Ophthalmology, June 2006 (Vol. 141, Issue 6, Pages 1160-1161) showed that even the most scrupulous care using bimanual small incision phaco could still only reduce the contamination rate to five per cent.

"Does phaco give a reduced bacterial contamination rate compared to ECCE? With a smaller incision a shorter surgical time, the anterior chamber continuously changed and irrigated, it should. Clear corneal incisions may be the problem in the fact that it does not," he added.

**Diagnosing endophthalmitis**

Modern molecular biological techniques can provide accurate species-specific identification of the causative microorganisms in eyes with endophthalmitis, even in cases that are culture negative, said Consuelo Ferrer PhD, VISUJ M, Instituto Oftalmológico de Alicante, Alicante, Spain.

In the past, a proportion of cases with extreme inflammation following cataract surgery would have been classified as hypopyon endophthalmitis, due to negative stain and culture findings. However, results with techniques like PCR analysis and DNA sequencing show that often such cases are due to infective organisms. They can also help identify the source of contamination and ensure that patients receive appropriate antimicrobial regimens, Dr Ferrer told the symposium.

The first step in determining the causative organism in cases of endophthalmitis is to obtain a stain from a sample of intraocular fluid. This technique can provide rapid information about the pathogen. However, its sensitivity is low in aqueous or vitreous samples. Furthermore, it does not reveal the identity of the pathogen, she pointed out.

Culture testing is the next step in diagnosing the cause of endophthalmitis, she noted. Identification of the microorganism with this test is based on the kind of culture medium the pathogens grow on, classic auxanographic techniques and the microscopic characteristics of the cultured cells.

However, sometimes cultures remain negative and may not really be negative for pathogens. Some causes for false-negative cultures include small sample size, sequestration of microorganisms on solid...
surfaces (e.g., intracocular lens, lens remnants, lens capsule), prior use of antibiotics and the fastidious nature of some microorganisms.

**Molecular diagnosis**

Molecular diagnostic techniques can overcome many of the drawbacks of stain and culture techniques because they only require a small amount of microorganism to give a positive result, and the microbes do not even need to be alive. Moreover, such techniques make it possible to identify the exact species of microbe involved, Dr Ferrer noted.

“The capacity for detection and identification of genomic material in any type of sample has constituted an enormous step in the field of medicine, allowing diagnosis of many genetic or infectious diseases based on the DNA sequence.”

Molecular diagnosis of ocular infections involves a technique that detects microorganisms by amplifying their DNA through polymerase chain reaction (PCR), she explained. The PCR technique requires a specialised laboratory and can determine within six hours whether there is microbial DNA present in the sample and whether it is of fungal or bacterial origin.

More specific identification of the organism requires DNA sequencing, a technique that differentiates between different species based on the nucleotide sequence of the amplified DNA. The procedure can take 12 hours to five days depending on the equipment available.

Dr Ferrer noted that all three types of tests, stains, culture and molecular biological tests should be carried out whenever possible due to the fact that each test has its advantages and disadvantages, some offering speed and sensitivity and others giving information not provided until now by molecular biological testing (sensitivity to antibiotics).

“PCR has proved to be a powerful tool for the diagnosis of endophthalmitis due to its higher sensitivity. Application of PCR and molecular methods can help us to discover new pathogens involved in ocular infections,” she added.

**Treatment of post-cataract endophthalmitis**

While prevention of endophthalmitis is better than cure, advances in vitreoretinal surgical technique and antibiotic regimens have greatly improved the visual outcomes of patients with this sight-threatening complication, said Zdenek J Gregor FRCS FRCOphth, Vitreoretinal Service, Moorfields Eye Hospital.

He told the symposium that while during the 1990s the rate of endophthalmitis following cataract surgery reached an all-time low of 0.087 per cent, between the years 2000-2003 the rate rose alarmingly to 0.265 per cent. Meanwhile, over the past two decades the percentage of patients with poor visual outcomes (<3/60) from the complication has fallen from 73 per cent to 11 per cent.

“Interestingly, the overall incidence of endophthalmitis is apparently rising perhaps as an unwanted effect of improving phaco technique”

Zdenek J Gregor FRCS FRCOphth

“Interestingly, the overall incidence of endophthalmitis is apparently rising perhaps as an unwanted effect of improving phaco technique. As for the possible reason for the improved outcomes of postoperative endophthalmitis, all I can think of is that it must be the result of people’s appreciation of the importance of the posterior segment surgeon’s role in redirecting the treatment at the retina, which after all ultimately determines the outcome of this condition,” he added.

**Vitrectomy vs. vitreous tap**

One decision the vitreoretinal surgeon must make when faced with a patient with endophthalmitis is whether to perform a formal pars plana vitrectomy or a simple vitreous tap, Dr Gregor said. He noted that, in theory, vitrectomy should be the preferred option.

Vitrectomy provides better yield for bacterial diagnosis, he pointed out. It also reduces traction on the anterior retina, and it fulfils the basic surgical principle of incision and drainage, eliminating all unwanted opacities from the media. In addition, vitrectomy allows for better circulation in the posterior segment of aqueous, which has antimicrobial properties. It also distributes antibiotics more evenly within the globe.

On the other hand, the landmark Endophthalmitis Vitrectomy Study (EVS) showed that vitrectomy only produced better results if the patient’s vision is light perception or worse. In patients with hand movements or better vitreous tap produced equivalent results.

Several recent advances in the field of vitreoretinal surgery may nonetheless make vitrectomy the preferred option in theory as well as practice in the majority of eyes, Dr Gregor maintained. For example, the improved technology now available provides wide angled viewing, which allows surgeons to perform a much wider and much more complete vitrectomy even in patients with no posterior vitreous detachment.

Furthermore, the increasingly popular practise of injecting steroids into the eye at the time of surgery may increase the safety and efficacy of such procedures. In theory, the steroids used are synergistic with antibiotics, as they reduce the intraocular inflammatory response and stabilise the blood-retinal barrier.

**New antibiotics**

Another finding of the EVS study was that intravenous antibiotics did not provide any benefit. However, new fourth-generation fluoroquinolones such as moxifloxacin may be effective in the treatment of endophthalmitis even when administered orally. The new agents are active against a broad spectrum of both Gram-positive and Gram-negative bacteria.

“Moxifloxacin has excellent ocular penetration, and high intravitreal levels may be obtained even after single oral administration. What is also important is that, in contrast to ciprofloxacin, there has as yet been no reported resistance,” he added.

Dr Gregor concluded by suggesting that the next 10 years will see further improvements in outcomes of patients with endophthalmitis as the use of laboratory tests such as PCR become more routine and vitreoretinal technology advances become more accessible.

**Steps to reduce postoperative infection**

By taking certain steps at each stage of surgery, it may be possible to reduce contamination of the eye during routine phacoemulsification and in the early post-operative period, said Samuel Masket MD, Clinical Professor, UCLA, Los Angeles, US.

“We have four opportunities to prevent infection in the routine procedures. We can decrease the microbes on the surface, we can prevent intraocular intraoperative contamination, we can, in fact, construct incisions that are hermetically sealed and we have the opportunity with intracameral and topical antibiotics to kill the microbes that may enter the eye at the time of surgery or after surgery,” he told the symposium.

Mr Masket noted that while povidone iodine is very effective in decreasing the amount of microbes on the surface of the eye, it is not effective against all pathogens and is somewhat toxic. Second and third generation fluoroquinolones are effective against a wider spectrum of bacteria and are better tolerated by the eye. They were, therefore, the topical agents of choice. However, pathogens have already begun to develop resistance to these agents, he noted.

Fortunately, newer fourth-generation fluoroquinolones have a molecular design that appears to make them not only more effective against bacterial pathogens but also less likely to generate resistant organisms. These agents may therefore supersede the older fluoroquinolones as topical agents, Dr Masket suggested.
Dr Masket emphasised that even with the best pre-operative regimens available it may be impossible to completely eliminate all of the microbes from the eye. However, the risk of contamination can be further reduced by very careful draping, isolating the lids and lashes, and by using aspirating speculums or tilting the patient so that tear fluid does not form a pool on the ocular surface, he said.

In addition, surgeons should reduce the number of times they enter the anterior chamber to a minimum and take utmost care to prevent capsular rupture, as vitreous is an excellent culture medium.

**Incision management**

Preventing postoperative contamination is largely a matter of incision construction and management. Several recent studies have indicated that clear corneal incisions can carry an increased risk of infection. However, the risk may be eliminated by ensuring that the incisions are hermetically sealed, Dr Masket said.

One reason scleral incisions may be safer is that they are typically less prone to dehiscence because of their square surface architecture. Clear corneal incisions tend to be more rectangular in their surface architecture because of the sharp blades used to create them.

On the other hand, it is possible to make clear corneal incisions that are hermetically sealed after surgery, Dr Masket said. This approach requires the surgeon to be very careful not to distort the incision during surgery. Maintaining stromal hydration throughout surgery and at the end of surgery is also important, as is establishing intraocular pressure at higher than normal levels 20 mmHg to help seal the incision shut, he noted.

"I've recently completed 50 consecutive eyes with evaluation from two to six hours after surgery and I have found zero evidence of hypotony and zero evidence of wound leakage using this strategy. It's somewhat compulsive but I think it's appropriate."

If this strategy is ineffective it may still be possible to eliminate contaminating organisms within the eye through the use of topical antibiotics, he pointed out. A recent study in which Dr Masket participated showed that topically applied moxifloxacin could achieve adequate intraocular levels to be bactericidal.

"That tells us that we can, in fact, with our present day antibiotics establish topical levels that may also prevent infection postoperatively."

**The cefuroxime story**

Per Montan MD followed Dr Masket's presentation with a description of how he and his team at St Erik Eye Hospital, Stockholm, Sweden, came to develop the intracameral antibiotic regimen that was used in the ESCRS Endophthalmitis Study.

"Like all stories it starts with trials and tribulations leading to a somewhat happier ending," he said.

In the early 1990s, Dr Montan and his associates noticed that they were having a high incidence (0.26 per cent) of endophthalmitis following cataract surgery. The Swedish team therefore searched for the best pre-operative culture medium.

Further confirmation of intracameral cefuroxime's efficacy has come from an analysis of Swedish national cataract register. Since 1999, over 400,000 patients have undergone cataract surgery with intracameral cefuroxime and the incidence of endophthalmitis dropped to 0.06 per cent.

To verify their results Dr Montan and his associates conducted a case-control study comparing the incidence of endophthalmitis before and after they adopted the cefuroxime regimen and analysing the subset of patients who were operated with phacoemulsification and receiving a silicone implant. They found that the incidence was 0.45 per cent with subconjunctival gentamicin, 0.53 per cent with topical chlorhexidine and gentamicin, but again only 0.07 per cent with intracameral cefuroxime.

"So my conclusions are that intracameral administration of antibiotics really makes a difference and that cefuroxime is safe to administer, has a reasonably broad spectrum and is a good candidate for this treatment," Dr Montan added.

"I've recently completed 50 consecutive eyes with evaluation from two to six hours after surgery and I have found zero evidence of hypotony and zero evidence of wound leakage using this strategy. It's somewhat compulsive but I think it's appropriate."

If this strategy is ineffective it may still be possible to eliminate contaminating organisms within the eye through the use of topical antibiotics, he pointed out. A recent study in which Dr Masket participated showed that topically applied moxifloxacin could achieve adequate intraocular levels to be bactericidal.

"That tells us that we can, in fact, with our present day antibiotics establish topical levels that may also prevent infection postoperatively."

**The cefuroxime story**

Per Montan MD followed Dr Masket's presentation with a description of how he and his team at St Erik Eye Hospital, Stockholm, Sweden, came to develop the intracameral antibiotic regimen that was used in the ESCRS Endophthalmitis Study.

"Like all stories it starts with trials and tribulations leading to a somewhat happier ending," he said.

In the early 1990s, Dr Montan and his associates noticed that they were having a high incidence (0.26 per cent) of endophthalmitis following cataract surgery.