



**Guidelines for managing
post-cataract surgery
inflammation**

Can we reach a consensus?

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Can we reach a consensus?

THE PANEL



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Since cataract surgery was first described, inflammation has always been accepted as a natural consequence of the procedure. Yet, despite the years of experience surgeons have had with this natural side effect, a clear consensus on how to treat it has yet to be agreed upon.

Some may find this quite startling; however, when one considers the different types of patient that are admitted for cataract surgery, the fact that there is no clear consensus on their therapeutic management becomes more understandable.

Who are the patients at risk?

A 'normal' cataract patient is a rarity these days. It is not uncommon for cataract patients to suffer from other conditions, including diabetes, macular disease, glaucoma, ocular vein occlusion, retinitis pigmentosa, or uveitis, to name just a few. And it is these patients who are also at a higher risk of suffering complications relating to inflammatory reactions from cataract surgery (see sidebar: **Defining the high risk patient**). As such, it is difficult to funnel all patients into one therapeutic regimen.

Furthermore, it is also difficult to put a precise value on the incidence rate of post-cataract surgery inflammation. Many studies set the figure at between 1.5 and 2%, though this does not take into account the diabetic population.

New technologies have combined with a continuing trend towards incision minimization (such as the MICS concept created by Professor Jorge Alió), and enhanced surgical techniques to lead to a distinct decrease in the intensity of inflammation and the number of patients suffering from inflammation-related complications following cataract surgery. Despite this reduction, inflammation continues to occur and it needs to be controlled. In particular, cystoid macular oedema (CME) is still recognized as one of the most common causes of poor visual outcome following cataract surgery.¹ Thus, the prevention and treatment of this condition is essential, particularly in higher risk patients.

Two key classes of agents are currently approved for use

in the treatment of post-cataract surgery inflammation: corticosteroids and non-steroidal anti-inflammatories (NSAIDs). Though both drug classes have suffered their own history of bad press, it appears that a corner has now been turned; newer formulations are now associated with improved safety, tolerability and good efficacy.

Whether these agents should be administered in combination or alone is still controversial, however, and in September 2008, a meeting of distinguished experts was convened to discuss the issue of post-cataract surgery inflammation. The objective of the meeting: to create guidelines for the effective management of inflammation following cataract surgery.

Prevention is key

“Prevention of inflammation is the goal; this means good patient selection, good preparation, good surgery, and a good postoperative therapeutic regimen,” said Professor Alió.

The fact that certain patients, these so-called high risk patients, are more prone to complications relating to post-cataract inflammation is undisputed. As such, it is essential that the surgeon performs all necessary preoperative evaluations in order to ascertain whether their patient falls into the high risk category, so that they can prepare their therapeutic strategy accordingly.

But is this always done in practice? “Sometimes I am referred patients that are experiencing postoperative complications, because they fall into the high risk group. I therefore suspect that some surgeons are not looking closely enough at their patients. For example, in cases of patients who are receiving IOP lowering drug medication; some surgeons fail to establish whether the medication is justified, should be adapted or discontinued,” stated Professor Marie-José Tassignon. “I would like to appeal to surgeons to select their patients carefully and to only operate if they are absolutely certain that their patients are well prepared for the surgery,” she added.

“The surgeon often works in isolation and ignores the clinical background of the patient, and this is a problem,” explained Professor Alió.

The panel agreed that a cataract surgeon must perform a full analysis of the patient preoperatively; this includes obtaining information relating to their medical history, existing conditions, and prescribed medications, to allow them to maximize their chances of preventing further complications.

The prostaglandin debate

“It is particularly important that we eliminate part of the patient’s existing therapeutic regimen if we believe that it

will increase the likelihood of complications,” reminded Professor Alió. He referred to a much debated example: prostaglandins.

Prostaglandins are prescribed as first-line therapy in glaucoma and ocular hypertension patients. As such, a significant portion of patients admitted for cataract surgery will be self-administering this therapy on a daily basis. However, controversy exists over whether or not these patients should continue this therapy when admitted for cataract surgery.

The reason for this relates to the knowledge of natural prostaglandin synthesis and its role in inflammation. During cataract surgery, natural prostaglandins are released from the iris and ciliary body and, from there, they migrate to the retina. Prostaglandins are then thought to contribute to the processes that lead to CME. In ‘normal’ cataract patients, this process, more often than not, is successfully combated by NSAID therapy. However, externally applied prostaglandin therapy places the patient at a higher risk of inflammatory complications post-cataract surgery.

“If I have a patient that is taking prostaglandin therapy and I do have other therapeutic options, then I will ensure that prostaglandin treatment is discontinued in favour of an alternative. I am very cautious with these patients,” said Professor Bahram Bodaghi. Professor Tassignon agreed.

“I find that it is useful to take intraoperative precautions in these patients; for example, I use low molecular weight heparin. This has been shown to reduce postoperative inflammation in prone patients. I also think this precaution is especially important in uveitic and diabetic patients,” said Professor Alió.

“I believe, and I have read in published papers, that preoperative prostaglandin treatment increases the incidence of subclinical CME.² On that basis, I cancel the therapy two weeks before surgery and prescribe an alternative medication as indicated,” explained Professor Alió. He reminded that cataract surgery is, indeed, one of the best forms of glaucoma therapy, as most patients naturally experience a postoperative decrease in IOP.

Professor Bodaghi referred to a recent paper published by the Moorfields group, which failed to demonstrate an increase in inflammation in uveitic patients receiving prostaglandins.³ “Again, this is ‘experience-based’ and further demonstrates that this issue is certainly not a clear-cut one,” he said.

Although standard practice for glaucoma patients receiving prostaglandin therapy has yet to be defined, the

“...preoperative prostaglandin treatment increases the incidence of subclinical CME”

Prof. Jorge Alió

general consensus is that a cataract surgeon must apply caution and discontinue treatment so long as a suitable alternative is available.

RECOMMENDATION

Caution must be applied in patients receiving prostaglandin therapy. Treatment should be discontinued if a suitable alternative is available.

Implementing guidelines: how hard can it be?

Glaucoma patients are just one example of a patient group that is at a higher risk of post-cataract surgery complications relating to inflammation. It is therefore necessary that a surgeon employs a different

postoperative regime for these high risk patients and this will differ to varying extents from the regime employed in 'normal', low risk patients.

Two classes of drug are currently indicated for the treatment of post-cataract surgery inflammation in all patient groups: corticosteroids and NSAIDs. Many studies have been published over the years examining the efficacy of these preparations, administered either alone or in combination, yet so far no clear consensus has been reached on

best practice for the management of post-cataract surgery inflammation.

Monotherapy vs combination therapy

"Admittedly, a different regimen must be employed for the two sets of patients that we have; namely the high and low risk patients. However, I firmly believe that both

sets of patients need to receive both topical corticosteroids and topical NSAIDs," affirmed Professor Alió. "We cannot ignore the substantial body of evidence that has shown the efficacy of combined topical corticosteroids plus NSAID treatment," he added.

According to Professor Alió, the patient is more exposed to problems relating to inflammation in the early postoperative period because of the surgical disruption to the blood ocular barrier. Because steroids block several aspects of the inflammatory process, including cyclooxygenase, the surgeon is able to control inflammation better. However, topical steroid use is associated with IOP spikes; hence long-term steroid treatment is not recommended. "It is best to intervene aggressively in the early postoperative period with steroids. These can then be removed from the equation. NSAIDs are a perfect addition to the treatment regimen as, not only are they better tolerated and induce fewer side effects than steroids, but they are also potent inhibitors of cyclooxygenase," explained Professor Alió.

NSAIDs alone might be good enough

"There are studies in the literature, however, which have shown equal efficacy of diclofenac administration alone, in comparison to a range of corticosteroids which were traditionally drugs of choice for the treatment of postoperative inflammation.^{4,5,6,7} As such, some surgeons only use NSAIDs to control postoperative inflammation," countered Professor Bodaghi.

"I agree that NSAIDs appear to sufficiently control inflammation in virgin eyes. In fact, Dr Miyake was the first to show the benefits of NSAIDs in the treatment of ocular inflammation.⁸ More recently, he performed a meta-analysis of all literature and concluded that the efficacy of NSAIDs in the treatment of post-cataract inflammation was unquestionable." added Professor Tassignon.

"Unless new evidence is presented, it appears that NSAID administration alone is insufficient in controlling post-cataract surgery inflammation"

Prof. Bahram Bodaghi

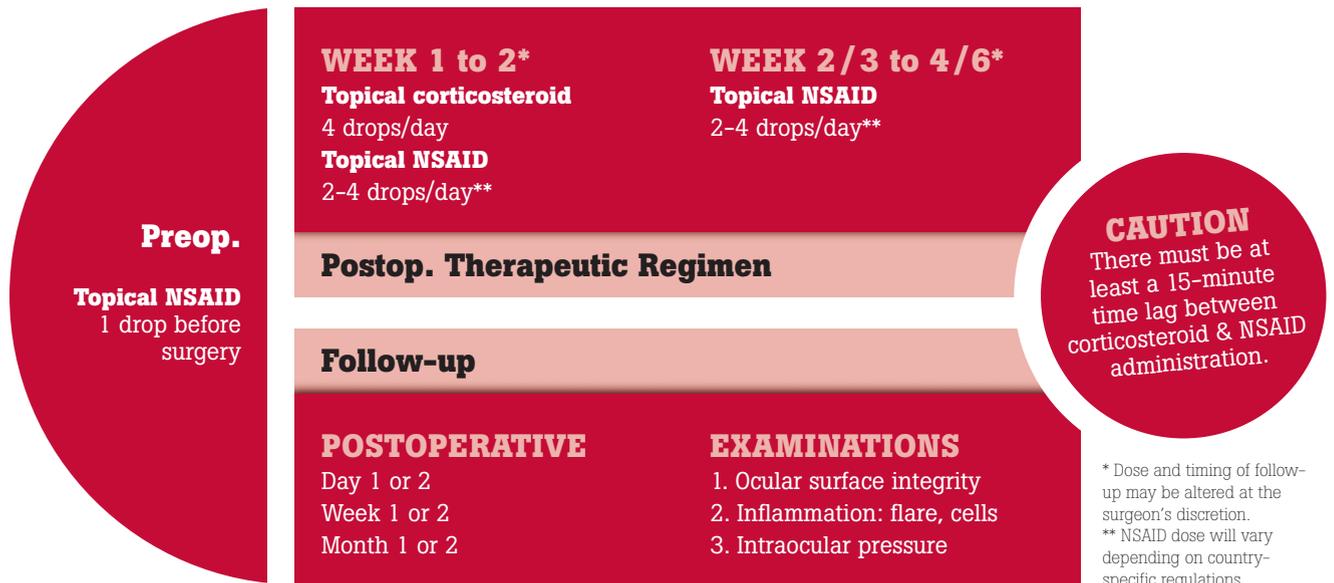
Defining the high risk patient

The high risk patient must be followed more closely than the 'normal' patient. The surgeon must adapt their preoperative, intraoperative and postoperative treatment regime as well as their follow-up protocol to adapt to the needs of the patient who is prone to inflammation-related complications post-cataract surgery. Those patients who are likely to be less tolerant of steroid or NSAID therapy are also included in the list below.

Patients with the following conditions fall into the high risk group:

- | | | |
|------------------------------|---------------------------------|----------------------------------|
| ■ Diabetes | ■ Retinitis pigmentosa | ■ Paediatrics |
| ■ Uveitis | ■ Macular oedema | ■ Ocular surface disease |
| ■ Glaucoma | ■ Epiretinal membranes | ■ Compromised corneal epithelium |
| ■ Pulmonary vascular disease | ■ Juvenile rheumatoid arthritis | ■ Corneal ulceration |
| ■ Ocular vein occlusion | ■ Juvenile idiopathic arthritis | |

Guidelines for treating the ‘normal’ patient



Furthermore, Dr Miyake's most recent study, clearly showed superior efficacy in patients receiving the topical NSAID diclofenac, in comparison to the topical corticosteroid betamethasone; after five weeks of surgery, 18.8% of diclofenac patients had CME, while 58% of patients in the betamethasone group were diagnosed with the condition.¹⁰ The flare test was also in favour of diclofenac and, as one would expect, IOP levels were higher in the betamethasone group. "But is this significant and do we need steroids too?" questioned Professor Tassignon. "The overall conclusion was that visual acuity was the same in both groups," she added.

Professor Bodaghi referred to a recent systematic literature review of randomized controlled trials evaluating the effects of NSAIDs in the treatment of CME following cataract surgery.¹¹ The study found no significant benefit of NSAID therapy in the treatment of acute CME, but a benefit was noted in the treatment of chronic CME. "Unless new evidence is presented, it appears that NSAID administration alone is insufficient in controlling post-cataract surgery inflammation," noted Professor Bodaghi.

The steroid safety net

Notwithstanding these conflicting reports, the experts were in agreement that a sufficient number of studies have been published, which show the benefits of combining the two drug classes, particularly in high risk patients.^{12,13} Along with their own substantial experience, they each opt to implement a treatment regimen that covers all patient subgroups, without naturally incurring

any treatment-related damage to the eye. This involves the co-administration of both medications.

"Steroids are much more efficient at treating the trauma-related inflammation that follows cataract surgery. I take a wider approach to my patients and I feel more comfortable using steroids. I admit that virgin eyes should react well to NSAID therapy alone, particularly preservative-free therapy; however, it is very difficult to administer this regimen because of the different patient populations that we treat," explained Professor Alió.

Professor Tassignon agreed, but she also conceded that perhaps some cataract patients are over-treated. "However, carefully controlled combined anti-inflammatory treatment does not, in our experience, harm the eye and, as a surgeon I believe it is better to be cautious. If a good protocol is followed carefully, you will gain good results," she assured. "If the issue of cost-effectiveness of therapy is raised, I would say that it is more cost-effective to administer CME preventative therapy than to treat CME, and this has been proven," Professor Tassignon emphasized.

RECOMMENDATION

Corticosteroid and NSAID therapy should be administered in combination to all patients.

Defining an optimum dosing schedule

The length of administration of each anti-inflammatory agent will, however, vary depending on the type of patient and their requirements.

“If we follow the IOIS recommendations, most uveitis patients will experience the same postoperative outcome as non-uveitic patients”

Prof. Jorge Alió

According to research, ocular barrier breakdown, a precursor to inflammation, continues for up to six weeks postoperatively. By that rationale, it seems conceivable that anti-inflammatory medication should continue to be administered during this time. “Patients will still be at risk of developing macular or sub-macular oedema in the second month, so six weeks of treatment should be the standard,” said Professor Alió.

Based on experience and with the use of microincision cataract surgery (MICS) in particular, Professor Bodaghi’s analysis has shown full restoration of the ocular barrier by one month. “Several studies do, however, show that patients are still at risk of developing CME within four to six weeks following surgery, even though they do not experience a decrease in visual acuity. Based on this, we are encouraged to continue therapy administration for up to six weeks,” said Professor Bodaghi.

The panel agreed that, in most patients, anti-inflammatory medication must be continued for up to six weeks; however, it is also agreed that certain patients may require extended treatment, depending on the complications present postoperatively. In these cases, the surgeon must be flexible, and adapt the regime to suit the patient.

In most cases, both Professor Bodaghi and Professor Alió administer topical steroid therapy, in combination with NSAIDs for one week postoperatively. After the first week, steroids are discontinued and NSAID therapy is continued for four to six weeks. In terms of dosing schedule, the doctors recommend steroid administration four times per day, and four doses of NSAID per day.

Professor Tassignon stated that, to improve patients’ compliance to postoperative treatment, she administers combination treatment throughout the course of the four-week postoperative period; however, she tapers the dose for practical reasons. She recommends four doses of each drug per day in the first week, and then she reduces this by one drop per week up until week four. Though she agreed that — since the patients are examined at week one — corticosteroids can be stopped earlier based on the clinical status of ocular inflammation.

Agreement was reached, however, on the importance of a time lag between therapy administration; the panel recommended leaving around 15 minutes between drops.

Cautionary measures for high risk patients

It was also agreed that NSAID and/or steroid therapy may need to be administered in high risk patients prior to surgery. In particular, macular oedema (ME) and uveitis patients must be given careful consideration.

With regards to uveitic patients, guidelines have been

Guidelines for treating the ‘high risk’ patient

<p>Preop.</p> <ul style="list-style-type: none"> ■ Topical NSAID and/or topical corticosteroids and/or other medication, as required. ■ Cancellation of other preoperative medications as required. <p>Regimen administered at the surgeon’s discretion. Surgeon aims for a preop. quiet eye.</p>	<p>Intraop.</p> <p>Additional medications, such as sodium hyaluronate, LMW heparin, acetazolamide, intraocular injections, etc., to be administered at the surgeon’s discretion.</p>	<p>WEEK 1 to 2*</p> <p>Topical corticosteroid 4 drops/day*</p> <p>Topical NSAID 2-4 drops/day**</p>	<p>WEEK 2/3 to 4/6*</p> <p>Topical NSAID 2-4 drops/day**</p>	<p>CAUTION</p> <p>There must be at least a 15-minute time lag between corticosteroid & NSAID administration.</p>
		<p>Postop. Therapeutic Regimen</p>		
<p>Follow-up</p>		<p>POSTOPERATIVE</p> <p>Day 1 or 2 Week 1 or 2 Month 1 or 2</p>	<p>EXAMINATIONS</p> <ol style="list-style-type: none"> 1. Ocular surface integrity 2. Inflammation: flare, cells 3. Intraocular pressure 4. Macular OCT 	<p>* Dose and timing of follow-up may be altered at the surgeon’s discretion. ** NSAID dose will vary depending on country-specific regulations.</p>

created by the International Ocular Inflammation Society (IOIS),¹⁴ which state that this set of patients must have a quiet eye for at least three months prior to cataract surgery and the quiet eye should be attained by any medication necessary, as prescribed by the uveitis specialist. "In line with these recommendations, I would administer anti-inflammatory treatment preoperatively. The good news is that, if we follow the IOIS recommendations, most uveitis patients will experience the same postoperative outcome as non-uveitic patients. These guidelines are very important," emphasized Professor Alió.

Unfortunately, such guidelines do not exist for ME patients. "We should therefore administer NSAIDs three days preoperatively as a preventative measure in these patients," Professor Alió recommended.

When questioned about the need for precautionary measures in Fuch's uveitis syndrome, the panel was divided. Although Professor Alió does not administer preoperative anti-inflammatory treatment, Professor Tassignon does administer NSAIDs for three days before surgery. For Professor Bodaghi, Fuch's patients may rarely develop severe anterior segment inflammation with a deposit of giant cells on the IOL surface. These rare cases do, however, need aggressive local corticosteroids.

Problems with paediatrics

"I agree that Fuch's patients must be monitored carefully; however, there are certain patients that I believe must be handled in the same way as uveitis patients, namely paediatric patients and those with juvenile idiopathic arthritis," Professor Bodaghi recommended. "A more aggressive anti-inflammatory regimen is necessary in these patients in order to ensure that the IOL is tolerated. For me, this is the worst population of patient," he admitted.

Professor Alió agreed that children are much more prone to developing synechiae, posterior capsular opacification (PCO), secondary glaucoma, and problems relating to the iris. "Early inflammation must be aborted in these cases; it is a tremendous problem as you have little chance to solve these complications later on," warned Professor Alió.

Intraoperative complications also occur in very high risk candidates and interventions employed by the panel members naturally vary depending on the situation. These often include, however, intraoperative administration of periocular, subtenons and intravitreal injections of therapy and very careful follow-up. In very serious cases topical medication is rarely increased significantly in order to avoid causing aggravation to the ocular surface.

"As a rule, if an eye is inflamed post surgery, our first job is to rule out infection, then to treat the inflammation and to prevent complications," confirmed Professor Alió.

Antibiotic controversy

Controversy also continues on the use of antibiotics following cataract surgery. With the trend continuing towards microincision surgery, some surgeons question which is the optimum type of anti-infective medication, whilst others are confused about the dosage requirements. Naturally, good surgical and hygiene techniques play a crucial role in the avoidance of infections, although antibiotic administration is still recommended.

Question marks also remain over which antibiotics are contraindicated for use with steroids.

"There have been problems with aminoglycosides and especially with tobramycin; this antibiotic has been shown to induce toxicity through its influence on matrix metalloproteinases. In fact, around 5% of patients that receive tobramycin will develop epitheliopathy during the postop period if administered for longer than 10 days," said Professor Alió. "It is therefore imperative that surgeons separate the use of the antibiotic from the steroid formulation and it must not be administered for longer than five to seven days," he stressed.

"Continuation of antibiotic therapy may explain the high number of complications with NSAIDs registered in France," explained Professor Bodaghi.

"Some surgeons administer antibiotics for much longer than is needed, sometimes up to a month," he said.

"Continuation of antibiotic therapy may explain the high number of complications with NSAIDs registered in France"

Prof. Bahram Bodaghi

Modern IOLs demand a good postop regimen

Irrespective of the debates that continue relating to therapeutic regimen, the fact remains that postoperative outcomes following cataract surgery continue to improve. Consequently, patient expectations have also risen. In order for patients to get the best outcome from their intraocular lens (IOL), particularly with the latest generation of lens, the use of anti-inflammatory medications is more important than ever.

"Postoperative inflammation significantly distorts the performance of accommodating lenses in particular, as well as the performance of multifocal lenses, because postoperative inflammation influences the incidence of PCO. In order to gain the best outcome from these lenses, early postoperative inflammation must be halted,

“If you continue steroid treatment for up to three weeks, you can pretty much guarantee that all of your patients will experience IOP spikes”

Prof. Jorge Alió

thus a higher dose of topical steroids is required in the first postoperative week in order to ensure a quiet eye, otherwise these lenses do not behave well,” advised Professor Alió. “As IOL technology continues to evolve, and more MICS lenses enter the market, the importance of these therapies will continue to grow,” he added.

In summary, the panel of experts agreed that anti-inflammatory medication was absolutely necessary. Although evidence has shown that NSAIDs alone are sufficient in virgin eyes, a combination strategy encompasses all patients, including those that are at high risk of postoperative complications.

While some high risk patients may require anti-inflammatory treatment in advance of surgery, the general consensus on postoperative treatment was that surgeons should administer a combination of steroids and NSAIDs; steroids at a dose of four drops per day for one week, and NSAIDs for four to six weeks post surgery at a dose of four drops per day. Doses will, however, vary depending on country-specific regulations (**see guidelines for treating the ‘normal’ and ‘high risk’ patient**). Anti-inflammatory medication is also increasing in importance with the advent of modern IOLs, particularly the accommodating and multifocal lenses. This trend will continue as new technologies enter the market. Antibiotics should also be administered for the first five to seven days following surgery.

RECOMMENDATION

Recommended dosing schedule is as follows:

Week 1 to 2: NSAID + corticosteroid therapy

Week 2/3 to 4/6: NSAID therapy only

Who should be following the patient?

Although the therapeutic schedule is important in ensuring a good postoperative outcome following cataract surgery, some may argue that the schedule of follow-up visits is equally important. It is at this point that the surgeon is more likely to have to administer alternative interventions should complications ensue.

By that rationale, each of the experts recommends that the cataract surgeon follows the patient. “The doctor is the natural owner of the patient. In Spain, this is standard practice, though this is controversial in other countries, such as the US,” explained Professor Alió. “Many medical

decisions are made in the postoperative period. Of course, it is easy to consider that around 90% of patients or even more will not require additional medical intervention postoperatively but, as doctors, it is our responsibility to look after our patients and to ensure that best practice is implemented,” he added. Professor Bodaghi and Professor Tassignon agreed.

The ideal follow-up schedule

The recommended follow-up schedule was similar for each of the panel members, with each emphasizing the importance of a minimum of three follow-up visits; the first occurring on postop day one or two, the second at week one or two, and the third visit at month one or month two. However, this timing sometimes needs to be adapted depending on the patient and their proximity to the clinic, as well if they fall into the high risk category, in which case a more careful follow-up regimen would be required.

“There are three main factors that a doctor must assess postoperatively: 1) ocular surface integrity, 2) inflammation, 3) IOP,” explained Professor Alió. He agreed that analysis of refraction and vision are important, however, these three crucial factors will inform the surgeon whether the patient has reacted badly to any of the medications administered.

After the three crucial follow-up visits, Professor Tassignon also tries to follow patients after six months, one year, and then yearly for the purpose of PCO (capsular healing) follow-up, “Patients tend to drop out after a year, which makes it difficult to conduct clinical studies,” she conceded.

The first follow-up appointment, which takes place one or two days after surgery, provides the surgeon with an immediate idea of how well the patient has tolerated the surgery. “The second follow-up appointment, which in my clinic takes place at one week, is very important to me for two reasons. Firstly, most acute cases of endophthalmitis take place between four and 10 days postop, and secondly, steroid-induced ocular hypertension is more pronounced within this period,” said Professor Bodaghi.

Professor Tassignon agreed. “An inflammatory reaction does not occur straight away; it is rare that you will witness this on the first postoperative day. So the second postoperative visit is very important. It is also very important to stress to patients that, if their vision is blurred in between follow-up visits, then they are to return to the clinic as a matter of urgency. In some cases, this blurring may be due to infection,” she added.

It was agreed that a minimum of three follow-up visits

at the one- or two-day, one or two-week, and one- or two-month time points were essential in order to secure a good outcome.

RECOMMENDATION

A minimum of three follow-up visits is recommended at day 1 or 2, week 1 or 2, and month 1 or 2.

Topical corticosteroids: the potent pacifier

In terms of the preferred therapeutics, molecules with strong anti-inflammatory activity, such as dexamethasone, are the topical corticosteroids of choice amongst each of the panel members.

Topical corticosteroids are potent anti-inflammatory and immunosuppressant agents that have a long and proven history of efficacy in the treatment of post-cataract surgery inflammation.

"Each corticosteroid molecule varies in terms of its penetration and efficacy.¹⁵ Dexamethasone alcohol and acetate preparations are incredibly penetrating and, as such are very efficacious in the treatment of intraocular inflammation," advised Professor Alió.

Enhanced penetration, however, is not without its drawbacks. Alcohol and acetate corticosteroid preparations are known to be associated with complications, the most frequently occurring being IOP spikes. "These drugs have to be handled with care. That's why their use must be limited to the first week to 10 days maximum. After this time, the risk of IOP spikes increases significantly," warned Professor Alió.

"In my opinion, it is necessary to administer these medications; each drop achieves a higher intraocular penetration allowing us to cover the peaks of inflammation better," said Professor Tassignon.

IOP spikes cannot be ignored

Although proven to be efficacious in the treatment of early post-cataract surgery inflammation, corticosteroids must be approached with caution. This class of agents can induce IOP spikes in 20% of patients, including diabetics, within the first seven days. "If you continue steroid treatment for up to three weeks, you can pretty much guarantee that all of your patients will experience IOP spikes," said Professor Alió.

A spike in IOP will not necessarily translate into problems for the patient because some patients, particularly low risk patients, can tolerate significant rises in IOP better than others. Hence, according to the panel, steroid medication must not be discontinued in those patients who have not reacted badly to a sharp rise in IOP. It is advised that a different approach should be

taken in those glaucoma patients who are at high risk of complications; for example, those at risk of optic atrophy before surgery.

How do we counter these increases?

"If corticosteroids have already been discontinued, I administer topical acetazolamide drops, which contain a carbonic anhydrase inhibitor, to patients who have peaks in IOP during follow-up, for one or two days. Not only does this agent lower IOP, but it has a positive influence on macular fluidics. This is usually very well tolerated," advised Professor Tassignon.

Professor Bodaghi, on the other hand, would normally discontinue dexamethasone treatment in those patients who experience IOP spikes, and he replaces it with another, less penetrating steroid. "I acknowledge the need for steroid therapy in post-cataract surgery patients and, as such, I prefer to find a less potent alternative. I will then closely monitor the patient to ensure that they do not develop secondary hypertension," he said.

Surgeons must approach the glaucoma patient with caution when administering steroids because of the influence of these agents on IOP.

"If I suspect that corticosteroids would cause a serious rise in pressure in my glaucoma patient, I would either ensure that the pressure is adequately controlled before surgery, or I will perform combination phaco-filtering surgery," added Professor Bodaghi.

Following the dosing schedule of four drops per day for one week, this treatment provides effective inflammatory control in the early period postoperatively. High risk patients, however — particularly those with glaucoma — must be monitored closely and, if worrying levels of IOP are reached in those at risk of complications, an alternative, such as a less penetrable steroid, or the addition of a compound such as acetazolamide, should be considered.

NSAIDs: the gentle giants

With regards to the NSAID of choice, again the panel members were united: preservative-free diclofenac.

The majority of NSAIDs bring about their anti-inflammatory effect by inhibiting the action of cyclooxygenase coenzyme (COX-1 and COX-2) activity on arachidonic acid. This class of agent is indicated for the treatment of ocular inflammation, including the control of

"I administer topical acetazolamide drops...to patients who have peaks in IOP during follow-up, for one or two days"

Prof. Marie-José Tassignon

intraoperative miosis, postoperative inflammation, CME, and inflammation due to conjunctivitis. It is also a potent ocular analgesic, indicated for use in the short-term treatment of pain associated with photorefractive keratectomy and corneal erosion.

Once the gold standard, indomethacin is a potent and efficacious NSAID, though problems relating to tolerance has led to a strong decline in its use in most countries. Now, diclofenac appears to dominate the market, particularly in Europe.

The black history of NSAIDs: dispelling the myths

Although NSAIDs have suffered a bumpy history because of reports of corneal melting and a subsequent market withdrawal in 1999, the consistent reports of safety with the newer class of agent should have bolstered surgeon confidence. And yet, many still approach this class of therapeutics with caution. In fact, a recent article published in the US publication *EyeWorld*, names NSAIDs 'the most underutilized [class of] drug on the market'.¹⁶ So it seems that some surgeons, particularly in the US, have yet to be convinced by the safety and efficacy of this drug class.

"The first generation of NSAIDs was produced with preservatives; the first available diclofenac formulations used sorbic acid or thiomersal — a mercury-containing preservative. The most recent preserved medication contains benzalkonium chloride," explained Professor Bodaghi. "At the end of the 90s, the American Society of Cataract and Refractive Surgery issued an alert noting a dramatic increase in the case reports of corneal injury.^{17,18} Most cases were related to a generic formulation (DSOS), which was ultimately removed from the market," he added. According to Professor

Bodaghi, there have been only a few other case reports associated with branded NSAIDs and these were usually linked with risk factors, such as high doses, misuse, comorbidity and co-administration with other ocular surface toxic products, such as certain antibiotics.¹⁹

"Admittedly, many surgeons in France are also cautious about using NSAIDs. Their concerns were further fuelled by recent reports, which linked the use of the NSAID nepafenac with corneal complications,"^{20,21,22} added Professor Bodaghi.

"Some patients do experience more itching and burning with NSAID medication though, in my experience, this is not the case with diclofenac and this is the main reason why it is dominant in the market. It is very well tolerated," Professor Alió interjected.

Concerns, however, still persist. "Every time a new product is introduced onto the market, we mustn't ignore any precautions that we used to take when administering this type of drug in the past. These agents are in the same family and so must be treated in the same way as before, unless otherwise stated," stressed Professor Bodaghi. He believes that it is this over-enthusiastic approach to treatment that has led to some cases of corneal meltings in France with the new formulation of diclofenac.

Compromised cornea contraindications

As a general rule, the panel agreed that NSAIDs should not be given to patients with corneal ulcers and should be administered with caution to patients with a compromised cornea. "A poor epithelium is a warning sign," stated Professor Alió.

"The doctor must ensure that the history of the patient is checked. Caution must be exercised in those patients who have a history of recurrent corneal erosions," added Professor Tassignon.

In patients with a compromised cornea or with dry eye, Professor Tassignon admits that she also includes sodium hyaluronate in her intraoperative regimen. Diclofenac is not contraindicated in these patients; rather, caution is applied and the patients are followed more carefully after surgery.

Preservatives are known to aggravate the ocular surface and thus are associated with conditions such as irritation and dry eye. Hence, a preservative-free treatment strategy is more suitable for the patient from a tolerance as well as from a convenience perspective.

With regards to the administration vehicle, at first, preservative-free medications were made available in monodose units. "Older patients have reduced mobility and the monodoses proved fairly difficult for them to manipulate," said Professor Tassignon. More recently, however, these medications have been made available in ABAK multidose containers, which are proving more popular amongst patients and surgeons.

Should we be starting therapy earlier in some?

In terms of dosing schedule, the experts agreed that NSAIDs should be administered preoperatively in high risk patients. Depending on the severity of the condition, this could mean administration of therapy for up to one

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Prof. Bahram Bodaghi

week before surgery. The ultimate aim is for a quiet eye. In virgin eyes, NSAIDs are applied around one hour before surgery and then at a dose of four drops per day thereafter.

In contrast to Professor Bodaghi and Professor Alió, Professor Tassignon prefers to taper her dose throughout the four-week follow-up period, because she has noticed that compliance after week one on a four-times daily regimen is very poor.

"We do not want to confuse patients with the therapeutic regime, certainly. I think we need studies that will define when we can safely halt treatment. Today, we do not have that conclusive evidence available," said Professor Alió.

Overall it was agreed that diclofenac is a well tolerated therapeutic. The few serious corneal adverse events that do occur could be largely avoided by good prescriptive practice and careful follow-up of patients at risk.

A plea to industry

Technology has evolved at an astounding pace in cataract surgery, particularly in the last five years, with the advent of new surgical techniques, phaco machines, devices, and IOLs.

As the intensity of postoperative inflammation has been decreasing, so too has the incidence of complications that ensue from undertreated inflammatory processes. Thanks to good therapeutic regimens, which should currently include corticosteroids and NSAIDs, surgeons are able to keep inflammation-related complications at bay for the vast majority of patients.

Notwithstanding this, there is always room for improvement and the way that therapeutics are administered and the frequency of administration will continue to improve.

"I would like to make a plea to industry for preservative-free steroids; our patients are elderly and have sensitive ocular surfaces, thus are prone to keratitis. These would be very valuable," said Professor Alió.

"Ultimately, in the future I would like to be performing eyedrop free surgery, primarily because I do not want to aggravate the ocular surface but also because patient compliance is an issue," he added.

According to Professor Tassignon, the answer lies in delivery vehicles, specifically a vehicle that can be placed inside the conjunctival sac, that will continuously deliver therapy. "I think that an insert or an IOL delivery system would provide the perfect solution. That way, if it causes problems, it can be removed," she said. "Of course, it is difficult to rely on patients to self-administer treatment.

Therefore, if we can avoid the patient's impact on their own safety with effective, preservative-free, intraocular solutions, this will provide the perfect solution," concluded Professor Tassignon.

Whilst we wait for industry to yield these futuristic solutions, it is agreed that post-cataract surgery inflammation must be treated and the complications related to inflammation must be prevented in all patients. In order to do this, surgeons must follow a careful therapeutic regime, which includes steroids and NSAIDs, administered over a period of four to six weeks, with at least three follow-up visits.

Surgeons must also identify those patients that are at high risk of inflammation and adapt their regime accordingly. Good patient selection, good preparation, a good surgical technique, a good therapeutic regimen, and close monitoring are all key ingredients for surgeons who want to implement best practice. ■

"...if we can avoid the patient's impact on their own safety with effective, preservative-free, intraocular solutions, this will provide the perfect solution"

Prof. Marie-José Tassignon

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Can we reach a consensus?

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