

Unique Applications of Steroids and NSAIDs

The latest formulations offer advantages in terms of on- and off-label applications.

BY SHERI ROWEN, MD

Thanks to the newest steroids and nonsteroidal antiinflammatory drugs (NSAIDs), along with our better understanding of ocular surface disease (OSD), we cataract surgeons can achieve better outcomes than ever before. As our awareness of OSD has increased, so has our need for safer, more effective ophthalmic preparations that are easier to administer and more comfortable for our patients. When deciding on our pre- and postoperative drug regimens, we therefore look to simplify the dosing schedule and reduce the preservative load. How have the most recently released agents made a difference?

EASE OF USE

The newest steroid agents, loteprednol etabonate ophthalmic gel 0.5% (Lotemax 0.5% Gel Drop; Bausch + Lomb) and difluprednate ophthalmic emulsion 0.05% (Durezol; Alcon Laboratories, Inc.), offer significant advantages over older formulations. For example, neither requires shaking, a real benefit because patients simply do not take this step even when instructed to do so.¹ The new formulations also offer uniform dosing: every drop contains a consistent concentration of medication. Although loteprednol gel and difluprednate are indicated for q.i.d. dosing, many of us have

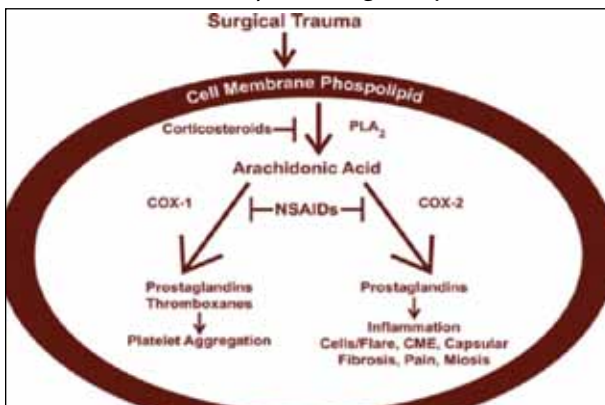


Figure. Arachidonic acid cascade.

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been tremendously successful with b.i.d. schedules after cataract and other surgeries, because less frequent dosing has increased compliance.

Also worth mentioning with regard to loteprednol gel are the addition of propylene glycol and glycerin and a decrease in benzalkonium chloride. These two known active demulcents and a lower amount of preservative have the potential to help maintain the integrity of the ocular surface, since many of us routinely use this agent to combat OSD.

The newest NSAIDs, bromfenac (Prolensa; Bausch + Lomb) and nepafenac (Ilevro; Alcon Laboratories, Inc.), also have enhanced formulations. Prolensa is actually halogenated amfenac, now available in a 3-mL bottle. Its pH has been lowered from 8.3 (Bromday) to 7.8, making the molecule more lipophilic to enhance corneal penetration. Prolensa's concentration is also lower than its predecessor Bromday, now at 0.07%. Ilevro is a modification of Nevanac (Alcon Laboratories, Inc.). At 0.3%, the concentration of the former is three times higher than that of the latter, and Ilevro contains guar gum, which prolongs its retention time on the cornea. These changes have maintained the efficacy of both molecules with q.d. dosing indications.

NEW APPLICATIONS

OSD and Meibomian Gland Dysfunction

The report of the International Dry Eye WorkShop in 2007 suggested the administration of antiinflam-

CASE EXAMPLE

One of my patients underwent routine uncomplicated cataract surgery but inadvertently discontinued her use of bromfenac ophthalmic solution 0.09% (Bromday; Bausch + Lomb) after 2.5 weeks. Four weeks postoperatively, she returned to the office with a significantly decreased UCVA of 20/50, and optical coherence tomography showed cystoid macular edema (CME; Figure). Within 2 weeks of reinstating the bromfenac as a b.i.d. dose, her CME had almost completely resolved, and her UCVA had improved to 20/20-2.

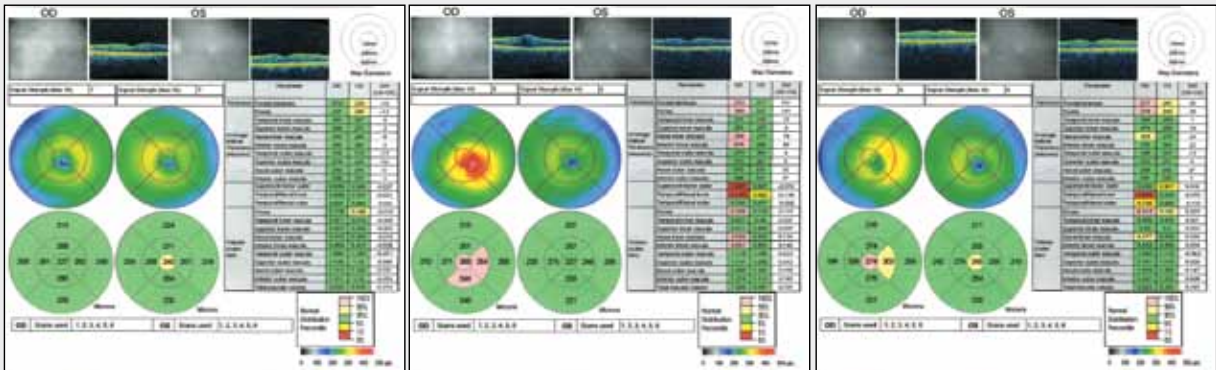


Figure. The preoperative optical coherence tomography scan was normal (A). The patient mistakenly discontinued bromfenac 2 weeks after surgery and was diagnosed with CME on postoperative day 36 (B). Two weeks of therapy with bromfenac nearly resolved her CME and significantly improved her UCVA (C).

matory agents for the treatment of patients with level 2 or higher dry eye disease.² Many of us therefore use a loading dose of steroids as a part of our regimens. Steroids also have a potential application in the treatment of meibomian gland dysfunction. A 2011 report by the International Workshop on Meibomian Gland Dysfunction suggested antiinflammatory therapy for patients with clinical signs and symptoms of moderate meibomian gland dysfunction, including ocular discomfort, itching, and photophobia.³

What makes steroids and NSAIDs effective in their mode of action? The inflammatory cascade involves sites that require specific blockade by steroids and NSAIDs. Together, these drugs effectively inhibit the phospholipase A2 and cyclooxygenase 2 enzymes, thereby preventing the conversion of arachidonic acid into prostaglandins (Figure). These lipid compounds stimulate (1) white blood cells, causing pain, and (2) vascular permeability, creating flare. This gives rise to the well-known cell-flare-pain reaction.

Because Lotemax has the unique properties of an ester, any steroid not bound to a glucocorticoid receptor is rapidly converted to an inactive metabolite, which explains the drug's excellent safety profile. Because the agent does not significantly increase IOP and cause cataract formation, many of us have selected it for longer-term use. The drug's availability in a new dose-consistent gel formulation with hydrating agents

may more effectively quiet inflammation of the ocular surface and lids as well as postoperative inflammation.

Cystoid Macular Edema

In an overview of pharmaceutical strategies to minimize complications after cataract surgery, Roger Steinert, MD, wrote that the exact incidence of cystoid macular edema (CME) remains unclear but that it is a frequent cause of vision loss after even routine cataract surgery.⁴ Studies suggest that the rate of clinical CME ranges from 1% to 12%⁵⁻⁸ and that the incidence of angiographic CME ranges from 9.1% to 39%.^{7,9-11} (See *Case Example*.)

Wittpen and colleagues found an association between small amounts of retinal thickening (>10 µm) and reduced contrast sensitivity after phacoemulsification, even in healthy patients with a low risk of CME.⁵ Mean visual acuity in patients with less than 10 µm of retinal thickening was approximately 20/22, but it worsened to a mean of 20/25 in patients with 40 µm of thickening or more. In other research, preoperative NSAID dosing improved the visual acuity of all study patients compared to that of controls.⁸

This broad category of subclinical CME may explain why some patients who have excellent visual acuity after cataract surgery complain that they see poorly. We are probably underdiagnosing minor CME. Because the cost of ophthalmic care is higher among Medicare

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patients who develop CME than those who do not,⁷ the cost of an NSAID is not sufficient reason for avoiding this method of prophylaxis.

CONCLUSION

The latest formulations of NSAIDs and steroids broaden our options for the prevention and treatment of surgical complications, and they have other off-label applications.

In addition, as recommended in the American Society of Cataract and Refractive Surgery’s recent alert, all viscous drops should be used after the placement of a bandage contact lens, not under it.¹² ■

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