Prostaglandin Analogs in the Cataract Surgery Perioperative Period

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INTRODUCTION

Since being introduced over a decade ago, the prostaglandin analog class of medications has revolutionized medical therapy for the glaucoma patient. These agents are commonly used as initial glaucoma therapy in areas of the world where they are readily available and affordable. The popularity of this class stems from several attributes including a high level of effectiveness in lowering IOP, convenient dosing, and predominantly harmless ocular and systemic side effects in most patients. One exception with regard to side effects has been the fear that these medications are contraindicated in special situations. Specifically, many case reports and retrospective analyses have implicated the prostaglandin analog class of medications as being linked to the development of postoperative cystoid macular edema (CME) in patients who have undergone cataract surgery. While some have postulated that this is a drug related side effect, a few clinical studies have shown that it is the preservative used with the medication, rather than the drug itself, which is the root cause of CME.¹ Another confounding factor is the variability of criteria for defining significant CME in the studies that have been reported.² As the prevalence of ocular hypertension and glaucoma in patients undergoing cataract extraction is high, almost all cataract surgeons routinely face the question of whether or not it is safe to use prostaglandin analogs during the cataract surgery perioperative period. To date, there have been no randomized control trials providing Oxford Level I evidence demonstrating causality, and a preferred practice pattern has yet to be published on this subject. This lack of consensus was highlighted in the results of a Royal College of Ophthalmologists survey conducted by Ahad and McKee which demonstrated that approximately 60% of physicians did not stop prostaglandin analogs following uncomplicated cataract surgery. Of those who did stop treatment, approximately half did so routinely while the other half did so only in patients deemed to be at high risk for postoperative CME.³ The purpose of this review is to summarize current available evidence with regard to this topic and to make recommendations for care based upon this evidence as well as the clinical experience of glaucoma experts.

HOW PREVALENT IS CME FOLLOWING CATARACT EXTRACTION?

While the prevalence of CME following cataract surgery would appear to be a relatively simple statistic to ascertain, the figure is largely dependant upon how one defines the condition. Clinical CME is characterized ophthalmoscopically as the presence of cystoids spaces in the macula, and has the lowest reported prevalence of all definitions.⁴ Clinically Significant CME, on the other hand, refers to decreased Snellen visual acuity associated with angiographic findings signifying this condition. The prevalence of clinically significant CME has been reported to be between 1% and 5%.⁵ This relatively large range is predominantly due to a variety of predisposing conditions which dramatically influence the likelihood of postoperative CME. A third definition, Angiographic CME, simply refers to the characteristic angiographic findings, regardless of impact on vision, and has been reported to occur as commonly as 30% following extracapsular cataract extraction.⁶ When reviewing the literature on this topic, it is imperative that one not apply data from studies describing one type of CME to another definition utilizing a different criterion. From a study design perspective, angiographic CMEs certainly an attractive end point, as the relatively high prevalence allows easier accumulation of evidence in support of or against causality. Additionally, this definition is the least subjective of the three mentioned above. On the other hand, clinical CME and clinically significant CME offer end points that are more relevant to patient outcomes relative to angiographic CME. Regardless of which endpoint is used in the definition, it is clear that a strict cause and effect relationship is difficult to establish given our rudimentary understanding of the disease process, along with the confounding factors commonly associated with the pathology of this condition.

CASE REPORTS

There are a plethora of reports in the literature that have attempted to establish a temporal association between the use

DISCUSSION AND RECOMMENDATIONS

One can make a good case that modern extracapsular cataract surgery, particularly when employing phacoemulsification, is the most commonly performed procedure for lowering IOP today. While there is great variability in what happens to the IOP among patients following cataract extraction with intraocular lens implantation, a drop in the average IOP has occurred after surgery in most study populations.^{19,21} Cataract surgery provides an excellent opportunity to stop glaucoma medications, adding them back only to the extent necessary in the postoperative period. In our clinical experience, a substantial proportion of patients who required prostaglandin therapy prior to cataract surgery will not need any glaucoma medications even in the long-term postoperative period.

There is no Oxford Level I highest-quality evidence demonstrating harm from the use of prostaglandin analogs prior to or after cataract surgery. Furthermore, the current literature has failed to demonstrate a clear association between these drugs and CME or ocular inflammation. Preservatives used with multiple topical glaucoma medications including, but not limited to prostaglandin analogs, may be more significant than active drug components in instigating the cascade of events that lead to the development of CME if indeed there is an association.²² While further study of the causality issue with regard to prostaglandins and CME is clearly needed, the low incidence of the condition, even with the use of these agents in the perioperative period lead one to question whether precise research funds might not be better served answering other questions. Regardless of the actual cause and effect relationship between prostaglandin analogs and CME, common sense dictates the discontinuation of these medications in the immediate postoperative period, particularly in patients with shorter or longer duration being recommended in eyes with preexisting risk factors that have been associated with postoperative ocular inflammation that is lesser or greater than increased risk of this complication. Such decision-making is made easier by the fact that prostaglandin analogs are less than ideal for lowering IOP during the immediate postoperative period. Medications such as alpha adrenergic agonists, beta-blockers, and topical and systemic carbonic anhydrase inhibitors (CAIs), all of which decrease the production of aqueous humor, are generally faster acting than prostaglandin analogs and are not mediators of inflammation, making them desirable postoperative IOP-lowering agents. In contrast, prostaglandin analogs are well known mediators of inflammation² further casting doubt on the appropriateness of using these agents, particularly in the early postoperative period. Although conclusive evidence that topical ocular prostaglandin use causes or exacerbates intraocular inflammation is lacking, most ophthalmologists would agree that using these agents in the early postoperative period is not optimal.

In cases where intraocular pressure can be temporarily controlled with other medications including beta-blockers, alpha

adrenergic agonists and topical or oral carbonic anhydrase inhibitors, we recommend discontinuation of prostaglandin analog therapy approximately 1 week prior to cataract extraction, particularly in eyes considered at high risk for the development of postoperative CME. Given that there is no evidence that such discontinuation decreases the likelihood of postoperative CME, the one-week time period is clearly arbitrary.

As the majority of IOP spikes after cataract extraction occur within the first postoperative week, commonly associated with retained viscoelastic combined with intraocular inflammation, we recommend that a prostaglandin analog should be the last pharmacologic choice for lowering IOP during this period for a variety of reasons. These transient IOP spikes can generally be controlled by aqueous suppressants such as alpha-adrenergic agonists, beta-blockers, or topical and oral CAIs, none of which have been postulated to cause intraocular inflammation. This claim is of course tempered with an admission of our lack of understanding of factors promoting postoperative inflammation, keeping in mind that there is evidence that preservatives used with such medications may play an important role in the pathogenesis of CME.

In cases where the risks of ocular pathology related to high IOP necessitate the use of prostaglandin analogs during the first few weeks of the postoperative period, the concomitant use of both topical NSAIDs and steroids is prudent. There is no good evidence that the use of adjunctive topical NSAIDs blunts the IOP-lowering effect of prostaglandin analogs.²³ Prostaglandins, if needed, are routinely resumed at approximately one month following cataract surgery, at which time these agents can replace aqueous suppressant therapy that was initiated in the early postoperative period. This one month hiatus from prostaglandin therapy is, once again, arbitrary with shorter or longer duration being recommended in eyes with postoperative ocular inflammation that is lesser or greater than average respectively. When pseudophakic eyes require long-term IOP-lowering therapy, however, prostaglandin analogs in most circumstances remain our preferred first-line agents after the first- postoperative month.

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