INTRAOPERATIVE MIOSIS IN CATARACT SURGERY

Reducing the associated risks has clinical and economic value.

BY ERIC D. DONNENFELD, MD; STEVEN M. SILVERSTEIN, MD; FRANK A. BUCCI JR, MD; AND DENISE M. VISCO, MD

Omidria (phenylephrine and ketorolac injection 1%/0.3%; Omeros) is the only intraoperative drug FDA approved for maintaining pupillary size and reducing postoperative pain. It is also the only approved product that contains a nonsteroidal anti-inflammatory drug for intraocular use. The clinical trials that provided the basis for FDA approval demonstrate compelling evidence of its efficacy, but there is a mistaken perception that Omidria is comparable to using intracameral epinephrine or phenylephrine. A prospective, randomized, double-masked, full-factorial trial shows, with statistical significance, that the agent is approximately fourfold more effective than intracameral phenylephrine at preventing miosis. The pivotal phase 3 clinical trials further confirm the product's effectiveness.[1-3]

A post hoc analysis of pooled results from the two phase 3 studies shows that just 4% of eyes treated with Omidria had a pupillary diameter of less than 6 mm at the time of lens implantation compared to 23% of eyes in the control cohort (both groups received standardized preoperative mydriatic and anesthetic treatment; data on file with Omeros). Only 2.1% of eyes treated with the product experienced pupillary constriction of 2.5 mm or greater compared to nearly 30% in the control group. These results were highly statistically significant ($P < .0001$). These studies also demonstrate that Omidria reduces postoperative pain for 10 to 12 hours after surgery. Half the number of control patients (7.2% vs 14.1%) reported moderate to severe pain at any time point up to 12 hours postsurgery, and 26% of treated patients reported being pain free compared to 17% in the control group. The pain score data are even more impressive when considering that patients using the agent received less treatment for pain, with 43% more control patients requiring postoperative pain medication.

These results are compelling, but ophthalmic surgeons all understand the necessary limitations of registration trials. Many doctors withhold judgment on new technology until they have the opportunity to try it in actual practice without the constraints of a clinical trial protocol. Early anecdotal reports on Omidria were positive, and some ophthalmologists, including those in high-volume cataract surgery settings, have now conducted their own case-controlled studies. There has also been a closer look at evidence in the literature around the incidence of adverse events associated with intraoperative miosis. Reports of these studies presented at the annual meeting of the Association for Research in Vision and Ophthalmology and the American Society of Cataract & Refractive Surgery help flesh out the product's clinical utility and allow surgeons to assess a new method of risk mitigation and the opportunity for cost savings in cataract surgery.

—Eric D. Donnenfeld, MD

The Impact of Intraoperative Miosis on Cataract Surgery Complication Rates

BY STEVEN M. SILVERSTEIN, MD

As cataract surgeons, we all have had to deal with intraoperative miosis. One study documented that 25% of cataract surgery patients with no identified risk factors will experience intraoperative miosis.[4] Fortunately, we know how to handle this phenomenon. Even so, these cases will be longer, outcomes may be adversely affected, and additional costs will be incurred. Despite steady improvements in technology and techniques over the past several decades, miotic pupils are still associated with often underappreciated surgical complication rates.[5,6]

In an effort to understand the impact of an FDA-approved intervention to prevent intraoperative miosis, I reviewed the literature to assess the rates of complications related to intraoperative miosis.[7] My colleagues and I conducted a literature review and meta-analysis that identified 40 studies published between 1998 and 2014 covering a total of 195,340 cataract procedures performed in the United States. We reviewed the publications to identify reports of relevant complications and extracted the necessary data to conduct the analysis. Using

appropriate meta-analytic methods, we calculated weighted estimates of complication rates.

The results of our analysis revealed that the most commonly reported perioperative complications associated with intraoperative miosis were posterior capsular rupture (4.2%), vitreous loss or leak (3.0%), and corneal edema (2.6%). The least frequent complication, zonular rupture, was reported at a rate of 1%. While the incidence of each individual complication is relatively low, the absolute numbers are significant, and taken together, complications such as these have a meaningful impact on the efficiency and cost of cataract procedures and on postoperative outcomes. Using a product that prevents intraoperative miosis allows surgeons to improve outcomes, increase efficiency, and reduce costs.

Reduced Need for Mechanical Iris Support

BY FRANK A. BUCCI JR, MD

The Malyugin Ring (MicroSurgical Technology) is an essential tool for managing poor dilation during cataract surgery. Because the use of pupil-expanding devices lengthens the procedure, increases facility costs, and potentially damages the delicate iris, preventing intraoperative miosis is preferable to managing it. Beginning in March 2015, I incorporated Omidria into my standard cataract procedure across a diverse patient population encompassing both routine and complex cases.

To evaluate the product's benefits, my colleagues and I reviewed 1,919 cataract procedures performed by the same surgeon. The review included a historical control group of 1,004 consecutive procedures completed prior to my adoption of Omidria and a treatment group of 915 consecutive procedures performed following its routine intraoperative use. The demographics as well as the frequency of use of a femtosecond laser in the two groups were statistically similar.[8] Intracameral injections of epinephrine were selectively used in the control group cases with intraoperative floppy iris syndrome (IFIS) or poorly dilating pupils, as determined by the judgment of the surgeon. All intracameral injections were performed just prior to use of a viscoelastic in preparation for the capsulotomy and just prior to the decision point regarding the use of a Malyugin Ring.

In the control cohort, I elected to use a Malyugin Ring 79 times (7.87%). In the Omidria cohort, the device was only deemed necessary in 27 eyes (2.95%), a statistically significant reduction in the need for this intervention ($P = .0001$). Use of the drug resulted in a threefold reduction in the need for mechanical iris support. This, in turn, improved procedural efficiency and reduced facility costs, clearly validating the decision to incorporate Omidria into routine clinical use.

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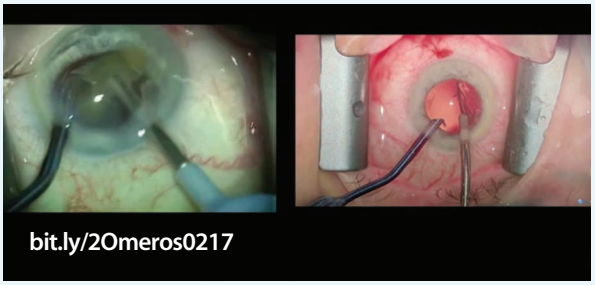
Robert Weinstock, MD, presents a side-by-side comparison of Omidria versus no Omidria.



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Clear Benefits in Patients at Risk of Intraoperative Miosis

BY DENISE M. VISCO, MD

Although intraoperative miosis is unpredictable, some factors such as a history of α-blocker use or the occurrence of miosis in the contralateral eye identify patients who are at increased risk of miosis during cataract surgery. When possible intraoperative miosis is identified as a patient risk factor, I prepare for active pupillary management with expansion devices to maintain adequate visualization during the procedure.

Omidria offers a new way to manage high-risk patients by preventing miosis. Patients with IFIS were specifically excluded from the FDA clinical trials, and there was no intraoperative active comparator. Shortly after adopting the drug in our practice, my colleagues and I conducted a retrospective case-controlled analysis of 46 cataract procedures during which intraoperative miosis was anticipated so as to determine whether the use of the product reduced the need for pupillary expansion devices. Specifically, our practice looked at how the agent's benefits compared to those of epinephrine.[9] To be included in the study, patients either demonstrated pupillary dilation of 5 mm or less after a pre-examination mydriatic regimen (tropicamide 1% and phenylephrine 2.5%) or had a history of IFIS in the fellow eye.

All patients received identical preoperative nonsteroidal anti-inflammatory drug and mydriatic regimens. Omidria was used in 10 cases, and epinephrine 1:1000 with sulfites was used in the other 36. These agents were added to the irrigating solution and delivered intracamerally throughout the case. I performed all of the surgical procedures.

The difference in intraoperative miosis between the two high-risk groups was dramatic. Patients who received the product

had very stable pupils, and none required the use of a pupil-expansion device. In comparison, fully half of the patients (18) in the epinephrine group required the use of an expansion device to maintain the pupil's diameter during the case ($P = .0036$).

Surgical times in the two groups also differed significantly. Mean surgical duration with Omidria was 10.1 minutes versus 14.33 minutes in the epinephrine group ($P = .0004$).

All of these cases were completed without complications, but avoiding pupillary contraction rather than managing it mechanically during surgery was definitely preferable. Despite the small sample size, Omidria demonstrated a clinically meaningful and statistically significant reduction in the use of pupil-expansion devices and in surgical duration in patients with known risk factors for intraoperative miosis.

Complications, Surgical Times, and Postoperative Outcomes

BY ERIC D. DONNENFELD, MD

For some time, ophthalmologists have used intracameral epinephrine to maintain mydriasis during cataract surgery. Setting aside medicolegal concerns about off-label, compounded agents for the moment, the availability of an FDA-approved intracameral agent raises the question of whether this new option provides any clinical advantage, either intraoperatively or postoperatively, over the prior approach.

Because comparative data were not available, a common obstacle to the adoption of Omidria was the comfort level that cataract surgeons had with the standard epinephrine regimen and its cost.

To attempt to settle the question of relative clinical value, my colleagues and I performed a retrospective case review of cataract procedures performed by four surgeons over a 3-month period at one of our surgicenters.[10] The study design compared patients receiving intracameral Omidria (n = 260) in the irrigation solution to those receiving similarly administered intracameral epinephrine (n = 381).

The group receiving the product had a lower incidence of complications (1.1% vs 4.5%; $P = .018$) compared to the epinephrine group. The use of Omidria also resulted in lower utilization of pupillary expansion devices in patients taking α-1 adrenergic blockers ($P < .001$). Across both groups, mechanical dilation was associated with a significantly higher complication rate (11.1% vs 2.5%; $P = .001$). In two age-matched cohorts, patients who received the agent had a significantly greater improvement in UCVA on postoperative day 1 than those who received intracameral epinephrine ($P < .001$). Omidria also resulted in a statistically significant reduction in age-adjusted surgical times compared with the procedures performed with epinephrine ($P = .049$). The reduction in complications and decreased surgical times are obviously primary benefits, but the improvement in visual acuity on postoperative day 1 is an important factor in patients' satisfaction with their surgical procedure.

Including this agent in the irrigating solution produced significant benefits for the surgeons and the patients in this study compared to epinephrine delivered in the same way. Compared to treatment with epinephrine, not only were Omidria cases associated with more than a fourfold reduction in complications, but they were also shorter and less likely to require the use of mechanical pupillary dilation—all resulting in cost savings for our facility. In addition, patients using the product had better visual outcomes the day after surgery. These results strongly support broad use of this product in cataract surgery. ■

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