

## Transzonular drug delivery during cataract surgery: Is dropless cataract surgery really beneficial?

Sir,

Cataract intraocular lens surgery is the most common procedure performed by ophthalmic surgeons worldwide. Cataract surgery is continuously evolving with innovative techniques, devices, and drug formulations are introduced every year. According to a recently published survey that aimed to document the existing pattern of practice of Indian ophthalmologists for antibiotic prophylaxis to avert endophthalmitis in cataract surgery, the eye was not prepared with 5% povidone iodine by all the participants and 83% of them utilized povidone iodine.<sup>[1]</sup> Majority of them used topical antibiotic before and after the operation. Nearly 46% opted for subconjunctival antibiotic after the surgery and 40% opted for intracameral antibiotic, mostly for high risk patients.<sup>[1]</sup> Moreover, this research also compared the data with that of 2014 survey results and it indicated the same decisions by Indian ophthalmologists for usage of intracameral antibiotic and antibiotic before and after operation. The authors of All India Ophthalmological Society (AIOS) members survey (published in the *Indian Journal of Ophthalmology*) concluded that the antibiotic prophylaxis practice pattern by

the Indian ophthalmologists is not too dissimilar from the practice in North American Ophthalmologists (ASCRS) though all ophthalmologists in India must be nudged to preoperative preparation of the eye with povidone iodine and discontinue the practice of postoperative subconjunctival and systemic antibiotic.<sup>[1]</sup>

While intracameral injections are increasingly used by ophthalmologists worldwide, several manufacturers are working on developing unique direct-delivery systems or devices (containing antibiotics and steroids) that can be used for cataract surgery cases during the postoperative period. A clinical trial of a punctal plug delivery system that elutes moxifloxacin (Ocular Therapeutix Inc, Bedford, MA, USA) exhibited a favorable safety and tolerability profile.<sup>[2]</sup> PolyActiva (Melbourne, Australia) had developed a biodegradable implant that releases levofloxacin over a 30-day period. The newly introduced technique of transzonular injection of antibiotic and steroid (described as dropless cataract surgery) is a move forward to limit or perhaps eliminate this medication regime. The technique of transzonular injection of moxifloxacin hydrochloride and triamcinolone acetonide is simple. It is done intraoperatively by injecting 0.2 cc of the TriMoxiVanc or Tri-Moxi (Dropless™; Imprimis Pharmaceuticals, San Diego, CA, USA) formulation into the anterior vitreous space using a 27-gauge blunt curved cannula. With the capsular bag and anterior chamber filled

with ophthalmic viscoelastic substance, the 27-gauge cannula is carefully introduced through the temporal clear corneal incision, and then directed by the operating surgeon beneath the iris nasally and over the peripheral edge of the anterior lens capsule. The tip of the cannula then passes between the zonular fibers, where the medication is then slowly injected by the surgeon. The medication in most cases can be visualized as it enters the anterior vitreous space posterior to the intraocular lens implant. Once injected, the medication remains sequestered in the anterior vitreous space, even as viscoelastic is subsequently removed from the capsular bag and anterior chamber. Intracameral injection of 0.15 cc of combination of 0.5% moxifloxacin and 0.1% dexamethasone (manufactured by Ocular Science, Manhattan Beach, CA, USA) is also being used by some surgeons in USA. Advantage of this clear solution is lack of transient blurring of vision associated with triamcinolone solution.

Tranzonular injection of antibiotics and steroids (dropless cataract surgery) technique is being utilized more and more by cataract surgeons around the globe. With manufacturers working to formulate optimum drug delivery system, it may be one of the significant developments for cataract surgery patients but is it really required, feasible, effective, and safe?

The usual cataract surgery medication schedule can be confusing and expensive for the elderly patients since it requires them to purchase and instill various eye drops, a number of times every day, for nearly 4–6 weeks post surgery. The main aim of this postoperative medication is the prevention of infection and inflammation after cataract surgery. Utilizing antiinflammatory agents and antibiotics post cataract surgery has proven to be highly effective to minimize inflammation (leading to cystoid macular edema) and infection (endophthalmitis). Until recently, this had been considered as an inconvenient yet acceptable method since there were no alternatives. In a recently published study, An *et al.*<sup>[3]</sup> reported that 92.6% cataract patients showed an improper eye drop administration technique, including missing the eye (31.5%), instilling an incorrect amount of eye drops (64.0%), contaminating the bottle tip (57.4%), or failing to wash hands before drop instillation (78.0%). These authors concluded that postoperative cataract patients inexperienced with eye drop use showed a poor instillation technique by failing to wash hands, contaminating bottle tips, missing the eye, and using an incorrect amount of drops.<sup>[2]</sup> This study has indicated that due to noncompliance, the patients' risk of endophthalmitis development as well as other complications drastically increases. In India, this issue can be more serious in high volume eye camp setting as lesser number of ophthalmic assistant/healthcare workers to educate these patients about after care and proper application of eye drops with few incidence of contamination of eye drops as a result patients using pin/needle to open them.

With dropless cataract surgery, the ophthalmic surgeon performs tranzonular injection of a combination of antibiotic and steroid intraoperatively during the cataract surgery. This technique only needs one administration and the patient is not required to purchase a number of eye drops for prophylaxis against inflammation and infection after being discharged.<sup>[4]</sup> This drastically decreases the compliance issues on part of patients.<sup>[5]</sup> Tranzonular injection of antibiotic and steroid was

initiated in the US and since its introduction, nearly 80,000 cataract operations have been performed using this adjunctive technique.<sup>[6]</sup> Published reports indicated that cataract surgery completed with the use of prophylactic antiinfective and antiinflammatory drugs delivered tranzonularly into the vitreous or topically provided similar safety in terms of intraocular pressure and corneal and macular edema, as well as similar effectiveness in terms of inflammation control, visual acuity, and patient comfort.<sup>[7-9]</sup>

The best option of performing dropless cataract surgery is by using one injection of antiinflammatory and antiinfective drugs (manufactured by Imprimis Pharmaceuticals and currently available in USA). A solution of three drugs approved by U.S. Food and Drug Administration is also utilized for isotonicity at a pH level, which is best compatible with the patient's eye. The compound includes vancomycin hydrochloride, moxifloxacin hydrochloride ophthalmic solution, and triamcinolone acetonide injectable suspension.<sup>[8]</sup> This compound solution eliminates the need to administer three or more eye drops after surgery to prevent/minimize infection and inflammation. Moreover, it also reduces the requirement of administering those eye drops repetitively for a course of 4–6 weeks as required with the drop current regime.<sup>[9]</sup>

Let us have a look at the pros of tranzonular drug delivery approach of, especially in terms of the high volume cataract surgery done in the developing world setting:

- Minimal or no eye drops needed in majority of the cases after cataract surgery.
- Postoperative regimen is simplified with no need for doctors to worry about patients wrongly using the eye drops. There is a decrease in compliance issues.
- The risk of application issues reduces with dropless surgery.
- Patients do not have to worry about purchasing prescription eye drops after cataract surgery.
- The overall cost is reduced.

According to reports on dropless cataract surgeries, as little as 5% of the patients needed drops with the Tri-Moxi experience, while the rest of the patients did not experience any problem.<sup>[10]</sup> It is a known fact that compliance of eye drops as well as poor adherence to medication after surgery are major issues. Moreover, the patients are also less likely to admit their poor adherence in hope of not disappointing their doctors, which results in worsening the problem. Therefore, tranzonular drug delivery system is highly beneficial in these cases.

While there are various benefits of dropless cataract surgery, it also comes with a few cons that must be considered by the ophthalmic surgeons and patients before opting for this technique:

- Floaters and cloudy vision have been reported by some patients a few days after surgery. This typically occurs because of opaque nature of the combination of drugs (moxifloxacin and triamcinolone acetonide) used. Cloudy vision is not reported with moxifloxacin dexamethasone combination preparation.
- The Tri-Moxi outcomes have not been researched enough.
- There are potential risks of retinal detachment and vitreous hemorrhage. However, such cases have not been reported as yet.<sup>[11]</sup>

It is too early to clearly determine the cons associated with dropless cataract surgery. There are of course some contradictions. It is best to avoid transzonular drug injection in cataract patients:

- Who underwent vitrectomy in the past?
- With capsular bag/zonular support system are unstable.
- Who are steroid responders?
- Who have glaucoma or are allergic to any component of the injection?

Although not available in India at present, latest transzonular injection of antibiotics and steroids can be suitable for numerous cataract patients, especially in developing countries where there are a vast number of patients for cataract surgery and there are lesser number of ophthalmic assistant/healthcare workers to educate them about after care and application of eye drops post cataract surgery. In a typical cataract surgery, the patients are supposed to use at least three eye drops that are instilled for 4–6 weeks postoperatively.<sup>[1]</sup> The instillation schedule of prescribed eye drops can be more challenging in cases with intraoperative complications or preexisting ocular (eg, glaucoma patients with 2 or 3 antiglaucoma medications) or systemic conditions (eg, difficulty in eye drop instillation by patients with rheumatoid arthritis). Nevertheless, this creates confusion among the patients as they are unable to keep up with the directions since various drops require differing times. There is also concern about cost, compliance, and preservative-induced corneal toxicity.

Dropless cataract surgery is also more beneficial for patients who get medication anxiety. Since majority of the patients undergoing cataract surgery are elderly, instilling three to four eye drops at different times every day can get rather challenging for them and their attendants. Many of these patients give up and do not take those prescribed medications and many simply forget to take them. With dropless cataract surgery, the patients need to put eye drops less frequently and can focus on their recovery instead. With no or minimal medications to purchase, the patients can save money. This eliminates the financial burden of buying medications for patients, especially the ones who have financial constraints. Clinical trials are under way to address the efficacy of transzonular drug delivery system. Indian pharmaceuticals are currently working to formulate a triamcinilone and moxifloxacin combination that can be used intraoperatively during cataract surgery.

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#### Conflicts of interest

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