Opinion

New frontiers of drug delivery innovation in cataract surgery

Opinion

Volume 8 Issue 3 - 2018

Suresh K Pandey,[1–3] Vidushi Sharma[1]
[1]SuVi Eye Institute & Lasik Laser Centre, India
[2]University of Utah, USA
[3]University of Sydney, Australia

Correspondence: Suresh K Pandey, SuVi Eye Institute & Lasik Laser Centre, C 13 Talwandi, Kota, Rajasthan, 324 005, India, Tel +91-935-141-2449,
Email suvieye@gmail.com, www.suvieyehospital.com

Received: May 24, 2018 | **Published:** June 12, 2018

Cataract-intraocular lens (IOL) surgery is the most common procedure performed by ophthalmic surgeons worldwide. Currently topical administration is the most common route of ocular drug delivery during cataract surgery. Despite its apparent easy accessibility, the eye is well protected from foreign materials and drugs by a number of very efficient mechanisms such as blinking, induced lacrimation, tear turnover, nasolacrimal drainage, which cause rapid removal of substances from the eye surface and by the cornea, which forms the physical-biological barrier. Most of the eye drop used during cataract surgery is not properly utilized in topical drug delivery system. Under normal condition the human eye can retain about 25–30µl of an ophthalmic solution; however after a single blink the volume is reduced to 7–10µl through nasolacrimal drainage which cause the drug to be systemically absorbed across the nasal mucosa or the gastrointestinal tract. A significant systemic loss from topically applied drugs also occurs from conjunctival absorption into the local circulation. Tear turnover, which can also be stimulated by factors such as pH and tonicity of the formulation, remove drug solution from the conjunctival cul-de-sac in a few minutes.

Problem with compliance of topical eye drop application led researchers to find out some alternative applications. Cataract surgery is continuously evolving with innovative techniques; devices and drug formulations introduced every year.[1] At present drug administration options during the cataract surgery include topical application (most common). Subconjunctival application is not used now. Intracameral Injection is reserved for antibiotic supplement. Biodegradable implant had shown considerable utility management of retinal disorders (refractory macular edema). After the success of sustained-release drug delivery systems such as Retisert (fluocinolone acetonide intravitreal implant 0.59 mg, Bausch+Lomb, USA,) and Ozurdex (dexamethasone intravitreal implant 0.7 mg, Allergan, USA), various drug delivery technologies are being developed to treat diseases of the eye. Encouraged by these, different ophthalmic issue spaces to implant these reservoir-based drug delivery systems are also being explored. Subcutaneous, subconjunctival, intracanalicular, intracapsular, transzonular and even suprachoroidal spaces have been researched at as potential sites for drug reservoirs or delivery system. Intravitreal inserts of brimonidine are being developed on the lines of the sustained-release dexamethasone PLGA platform for the management of geographic atrophy due to age-related macular degeneration and also as a neuroprotective modality in the management of glaucoma.

Intracameral injections are increasing in use by ophthalmologists worldwide; several manufacturers are working on developing unique direct-delivery systems or devices (containing antibiotics & 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, USA) exhibited a favorable safety and tolerability profile.[2] PolyActiva (Melbourne, Australia) had developed a biodegradable implant that releases levofloxacin over a 30-day period. These experimental procedures are currently being explored in animal/clinical studies. In this editorial, the authors will focus about the newly introduced clinical technique of transzonular injection of antibiotic and steroid (described as dropless cataract surgery) that is an advancement to limit or perhaps eliminate the post-operative 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, 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 (OVD), 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 IOL 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 percent moxifloxacin and 0.1 percent 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 four to six weeks post-surgery. The main aim of these postoperative medications is the prevention of infection and inflammation after cataract surgery. Utilizing anti-inflammatory agents and antibiotics post cataract surgery has proven to be highly effective to minimize inflammation (leading to cystoid macular edema) and infection (endophthalimitis). Until recently, this had been considered an inconvenient, yet acceptable method since

there were no alternatives. In a recently published study, An and associates[3] reported that 92.6% cataract patients have 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.[2] This study has indicated that due to non-compliance, 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 ophthalmologist performs transzonular injection of a combination of antibiotic and steroid intra-operatively 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.[4] This drastically decreases the compliance issues on part of patients.[5] Transzonular injection of antibiotic and steroid was initiated in the United States and since its introduction, about 80,000 cataract operations have been performed using this adjunctive technique.[6] Published reports indicated that cataract surgery completed with the use of prophylactic anti-infective and anti-inflammatory drugs delivered transzonularly 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.[7–9] The best option of performing dropless cataract surgery is by using one injection of anti-inflammatory and anti-infective 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.[8] 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 four to six weeks as required with the drop current regime.[9]

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

i. Minimal or no eye drops needed in majority of the cases after cataract surgery.

ii. Post-op regimen is simplified with no need for doctors to worry about patients wrongly using the eye drops. There is a decrease in compliance issues.

iii. The risk of application issues reduces with dropless surgery.

iv. Patients don't have to worry about purchasing prescription eye drops after cataract surgery.

v. 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 didn't experience any problem.[10] 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 hopes of not disappointing their doctors, which results in worsening the problem. Therefore, transzonular 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:

I. 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.

II. The Tri-Moxi outcomes have not been researched enough.

III. There are potential risks of retinal detachment and vitreous hemorrhage. However, such cases haven't been reported as yet.[11]

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 tranzonular drug injection in cataract patients:

i. Who underwent vitrectomy in the past?

ii. With capsular bag/zonular support system are unstable.

iii. Who are steroid responders?

iv. 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 four-six weeks postoperatively.[11] The instillation schedule of prescribed eye drops can be more challenging in cases with intra-operative complications or pre-existing ocular (e.g. glaucoma patients with 2 or 3 anti-glaucoma medications) or systemic conditions (e.g. difficulty in eye drop instillation by patients with rheumatoid arthritis). Nevertheless, this creates confusion amongst the patients as they are unable to keep up with the directions since various drops require differing times. Also 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 don't take those prescribed medications and many simply forget to take them. With dropless cataract surgery, the patients need to put eye drop 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

Citation: Pandey SK, Sharma V. New frontiers of drug delivery innovation in cataract surgery. *Adv Ophthalmol Vis Syst.* 2018;8(3):176–178.
DOI: 10.15406/aovs.2018.08.00297

efficacy of transzonular drug delivery system. Indian pharmaceuticals are currently working to formulate a triamcinilone and moxifloxacin combination that can be used intra-operatively during cataract surgery.

Acknowledgements

None.

Conflict of interest

The author declares that there is no conflict of interest.

References

1. Jonas JB, Kreissig I, Budde WM, et al. Cataract surgery combined with intravitreal injection of triamcinolone acetonide. *European J Ophthalmol*. 2005;15(3):329–335.
2. Chee SP. Moxifloxacin punctum plug for sustained drug delivery. *J Ocul Pharmacol Ther*. 2012;28(4):340–349.
3. An JA, Kasner O, Sarnek DA, et al. Evaluation of eyedrop administration by inexperienced patients after cataract surgery. *J Cataract Refract Surg*. 2014;40(11):1857–1861.
4. Liegner JT. Innovations in Ophthalmology: Dropless Cataract Surgery; A steroidantibiotic combination can replace expensive eye drops, save money, and ensure compliance. *Cataract Refract Surg Today*. 2015. p. 70–71.
5. Schweitzer J. Dropless Cataract Surgery Offers Benefits for compliance Patients, Providers; Convenience and improved are among the advantages. *Advanced Ocular Care*. 2015. p. 28–29.
6. Lindstrom RL, Galloway MS, Grzybowski A, et al. Dropless Cataract Surgery: An Overview. *Curr Pharm Des*. 2017;23(4):558–564.
7. Jeffrey T. Innovations in Ophthalmology: Dropless Cataract Surgery. *Cataract & Refractive Surgery Today*. 2015. p. 70–71.
8. Fisher BL, Potvin R. Transzonular vitreous injection vs. a single drop compounded topical pharmaceutical regimen after cataract surgery. *Clinical Ophthalmology*. 2016;10:1297–1303.
9. Rhee MK, Mah FS. Cataract Drug Delivery Systems (Dropless vs. Nondropless Cataract Surgery). *Int Ophthalmol Clin*. 2016;56(3):117–136.
10. Stringham JD, Flynn HW, Schimel AM, et al. Dropless Cataract Surgery: What Are the Potential Downsides? *Am J Ophthalmol*. 2016;164:8–10.
11. Kessel L, Tendal B, Jorgensen KJ, et al. Post-cataract prevention of inflammation and macular edema by steroid and nonsteroidal anti-inflammatory eye drops: a systematic review. *Ophthalmology*. 2014;121(10):1915–1924.