Hyaluronic Acid Release from an Intraocular Lens to Diminish Dry Eye Symptoms After Cataract Surgery

Chloe Smith and Mignon Le Roux

Abstract
Intraocular lens replacement surgery is becoming increasingly popular as the population ages. A common postoperative complication is dry eyes, which causes significant discomfort to the patient and may impair the visual recovery after surgery. Intraocular lenses have been used as a drug delivery system in the past and their modification to release hyaluronic acid (HA) may be beneficial to patients recovering from surgery. This may augment the eye’s natural ability to create moisture. We propose to study the release of HA and Rapamycin (RAMPA), a common immunosuppressant used in cataract surgery, via an intraocular lens delivery system. The release quantity, rate, and longevity of HA and RAMPA will be assessed using spectrometry, HA Enzyme-Linked Immunosorbent Assay and LC-MS/MS. The following study would be the first step in creating a HA-releasing polymer sprayed intraocular lens with the aim of alleviating post cataract surgery dry eyes (xeropthalmia).

Keywords: Cataracts, Intraocular Lens, Dry Eyes, Hyluronic acid, Rampamycin, Drug Delivery

Scientific background
In an aging population, it is important to focus research towards helping people age comfortably. 82% of visually impaired individuals are above the age of 50 with cataracts being the second leading cause of visual impairment (Hashemi et al. 2017). Cataract formation is the clouding of the lens, over time, due to the degradation of lens proteins. This may lead to blurred vision and blindness. This condition is commonly treated with surgery that consists of removing the cloudy lens from the lens capsule and inserting an artificial lens (Allen and Vasavada, 2006). Although the surgery has a high success rate, a persistent postoperative complication is induced or worsening dry eyes. A study led by Dr. Cal Roberts showed that 87% of cataract patients must use eye drops at least once daily and 53% of patients reported a burning sensation in their eyes daily within the first month post-surgery. Unfortunately, even with the use of medications or eye drops multiple times daily, many patients still report discomfort and adverse effects from medication, resulting in the exacerbation of the dry eyes. Additionally, dry eyes after surgery may impair the visual outcomes and recovery time (Stephenson, 2007).

An alternative treatment to postoperative dry eyes is the release of HA from an intraocular lens (IOL) which is inserted during cataract surgery (Kozarsky, 2018). IOLs can be used as drug delivery systems releasing chemicals into the eye, like immunosuppressants or antibiotics (Wertheimer et al. 2017). HA, known for its water retention capabilities, is commonly used in dermatology and to treat dry eyes (Papakonstantinou, Roth and Karakiulakis, 2012). HA is found at high concentration in the vitreous and aqueous humor, coating the epithelial cells of the eye. In rabbits and marine subjects HA is effective against dehydration and tear film instability. HA also increases the number of goblet cells, which secrete mucus within the eye. Research indicates that HA stimulates epithelial migration, which protects corneal epithelial cells from destruction and apoptosis, improving retinal image quality over time (You, 2018). The release of HA from an IOL could augment the eye’s natural ability to create moisture, diminishing dry eye discomfort and potentially improving long-term outcomes.

Purpose
We propose the following study to analyze the release of HA and RAMPA via an IOL drug delivery system. This may be a solution to relieving short-term postoperative dry eyes.

Hypothesis
Active HA and RAMPA will be present at consistent levels for at least 12 days from the time of submersion.

Significance
In 2014, around 145000 cataract surgeries were performed in Ontario (The Canadian Association of Optometrists, 2015). As the population is aging, it has been predicted that 250000 cataract surgery will be performed annually by the year 2026, rising by 43% (The Canadian Association of Optometrists,
2015). Decreasing morbidity and improving long term outcomes are crucial to the ever-increasing patient population that will require this surgery. This indicates that the frequency of cataract surgeries is continuing to increase and therefore, developments that decrease the unwanted symptoms (like dry eyes) and that improve the long term benefits of the surgery are crucial to modern medicine.

Methods
Twenty-five PMMA IOLs will be obtained from Suzhou Medical Instrument General Factory (Suzhou medical Instruments Factory, no date). This experiment consists of 5 groups, each containing five IOLs exposed to different conditions. The processed lenses are provided by East China University of Science and Technology (Shanghai, China) (East China University of Science and Technology, no date). Group I lenses (PMMA) acts as a control to show the aggregation of epithelial like cells on the IOLs without any spray coating. Group II lenses (PMMA-PGLA) were treated with PGLA, a polymer which acts as scaffolding for drug delivery. The IOLs’ edges are sprayed with 1% solution of PGLA (lactide/glycolide ratio 50/50) in chloroform to form a layer approximately 2mm thick (Papakonstantinou, Roth and Karakulis, 2012). In group III lenses (PMMA-PGLA-HA), the edges are sprayed to the same thickness and concentration. However, HA is added to solution such that approximately 40µg HA and 10µg PGLA are deposited on the IOLs. In group IV lenses (PMMA-PGLA-RAMPA), the same procedure as group III was used; however, HA is replaced with RAMPA. Finally, group V lenses (PMMA-PGLA-HA-RAMPA) were treated similarly as groups III/IV; however, HA and RAMPA are added such that approximately 20µg RAMPA, 20µg HA, and 10µg PGLA are deposited on the IOLs (Liu et al. 2008).

Once all IOLs are prepared, each IOL is suspended in 10mL sample of synthetic aqueous humour solution, prepared as outlined in Macri A., et al. for 21 days (Macri, 2015). At time of submersion, a baseline of solute concentration is set using a 1mL sample of the solution being analyzed by 240 nm spectrometry (Li, 2017). Moreover, a 1mL sample of the solution is acquired for the following analyses, every 3 days and replaced with 1mL fresh synthetic aqueous humour. First, using the 240nm spectrometer, the change in solute concentrations will be assessed to indicate drug release from IOLs. Furthermore, 100µL of the sample is analyzed using HA Enzyme-Linked Immunosorbent Assay (ELISA) to determine the level of HA in solution (Hyaluronan Competitive, no date). Lastly, 200µL of the remaining sample is analyzed using LC-MS/MS method, as described by Mueller and Rentsch in 2012, to detect and quantify RAMPA concentrations (Mueller and Rentsch, 2010). The condition of the IOLs are also qualitatively observed and recorded for any opaqueness or discoloration indicating molecular deposition. The data is then graphed (Brancha, 2012) and statistically analyzed to assess the rate and longevity of drug release from the synthetic polymer coating. This study may be the first step in developing a combination drug delivery system from polymer sprayed IOLs. HA released from IOLs in the context of current cataract surgery may prove to be an effective short-term treatment for post-operative dry eyes.

References
East China University of Science and Technology [Online]. Available at: https://www2.ecust.edu.cn/_t41/main.htm (Accessed 22 November 2019).


You, I.C. et al. (2018). ‘Comparison of 0.1%, 0.18%, and 0.3% Hyaluronic Acid Eye Drops in the Treatment of Experimental Dry Eye’. J Ocul Pharmacol Ther, 34(8).