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The Challenge of Mature Cataracts in the Third World

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In cataract surgery, the primary anatomic goal is to remove the cloudy human lens in a way so as to preserve the surrounding clear support capsule. This delicate, transparent capsule is suspended inside the anterior half of the eye by a ring of tiny peripheral support ligaments called "zonules". If successfully preserved, the capsule constitutes the best means of supporting the permanent artificial replacement lens implant.

Under microscopic visualization, a circular opening is torn in the front of the capsular bag (anterior capsulotomy). The components of the cataractous lens are then removed in several stages. The major portion of the elderly lens consists of a large solid "nucleus". This is surrounded by softer semi-solid elements that can be aspirated. The intact capsular bag is temporarily inflated with a transparent viscous gel to allow implantation of the artificial intraocular lens (IOL). Each IOL model is available in approximately 40 different optical powers, of which one has been selected in advance, based upon the custom optical requirements of the individual's eye.

Removing the bulky, solid nucleus in one piece requires a large incision to be made at the edge of the cornea ("limbus"). This extends for five clock hours of the corneal circumference, and must be closed with 8 - 10 sutures (10-0 Nylon) following IOL implantation. Because of the large incision size and location, a periocular local anesthetic must be injected.

The instability of large ocular incisions delays physical and functional rehabilitation for several reasons. Valsalva maneuvers and physical exercise must be limited for several weeks. The sutures often distort the optically uniform curvature of the cornea, thereby inducing or increasing astigmatism. Sutures are usually not removed until 6 weeks have passed. The refraction used for new eyeglasses may not be stable for 8 weeks, and the large incision usually causes a gradual but progressive astigmatic increase over a period of 2 - 3 years, necessitating more frequent future spectacle adjustments.

Cataract Surgery in the United States - The State of the Art

For the past decade in the industrialized world, small incision cataract surgery has become the standard. The incision can be kept to a 3-3.5 mm size by using ultrasound technology (phacoemulsification) to fragment and liquefy the nucleus into an emulsate that can be aspirated. The phacoemulsification handpiece operates a specially designed, 19-gauge aspirating cannula. On demand, this sharpened tip ultrasonically vibrates 50,000 cycles/sec resulting in emulsification of the solid nuclear material. The liquified lens elements are aspirated out.

Foldable intraocular lenses made of either silicone or acrylic plastic are now the preferred design. Since the standard IOL optic is 6 mm in diameter, these lenses can be folded and implanted through the 3-3.5 mm incision. Folding can be accomplished either with special forceps or by rolling the lens optic and injecting it into the capsular bag where it is allowed to unfold, unadulterated into its original configuration. Each foldable IOL model has its own dedicated injector instrumentation.

The ability to perform the entire lens removal and IOL implantation through a tiny 3-3.5 mm corneal incision provides many predictable advantages. The surgery can be performed using topical anesthesia, avoiding the discomfort and potential needle complications of a regional anesthetic block. Less intraoperative sedation is required. An incision of this size is small enough to be placed through clear cornea. This bloodless incision, and the elimination of any anesthetic injection, precludes hemorrhagic complications altogether. Anticoagulants need not be discontinued for this method of cataract surgery.

Small incisions maintain a closed system for intraocular surgery. This is safer in terms of certain potential intraoperative complications, and in the event of a restless or moving patient. With small, self-sealing incisions of this size, postoperative wound complications have been virtually eliminated. Typically, no physical restrictions are placed on the patient's activity level. Since the anesthetic is topical, no bandage is necessary following surgery and the patient has some functional level of vision immediately after surgery. Cosmetically, there is usually no bruising or other visible evidence of the surgical procedure. Compared with larger incisions, small incisions have been shown to induce less intraocular inflammation.

A <3.5 mm, self-sealing cornea incision does not require sutures, and is so small that it does not change the natural corneal contour. The postoperative refraction for glasses is therefore stable by two weeks, and no unwanted surgically astigmatism is introduced. This is true both in the short term and long term, in contrast to the larger incision. Decreased astigmatism means better uncorrected visual acuity (without glasses). Overall, state-of-the-art small incision cataract surgery means almost immediate visual and physical rehabilitation of the patient, and better long term results in terms of avoiding unwanted surgically-induced astigmatism.

In Third World settings, such as most of China, the main problem is one of access to care, such as ocular microsurgery. In China, the number of people reversibly blind from cataracts as they await surgery is increasing by one million additional patients per year.

As unoperated cataracts advance over time, the nucleus enlarges and hardens. Once this process advances enough, it significantly increases the complexity and complication rate of small incision surgery. Depending on the individual surgeon's level of skill, training, equipment, and experience, the advanced cataract eventually reaches a stage where large incision cataract surgery becomes safer than the small incision method. At their most advanced stage, such cataracts turn white and, having become completely opacified, are designated as "mature" cataracts. At this point, the eye is functionally blind. These cases are extremely challenging to perform safely through a small incision, and although uncommon in the West, they are very common in the Third World.

With the delayed timing of cataract surgery leading to so many advanced and mature cataracts, and given the limitations in the availability of equipment, surgical training and experience, the great majority of cataracts in China and the Third World are removed using the large incision method. However, at larger eye centers in major cities, leading Chinese surgeons are becoming more and more adept at small incision cataract techniques.

Significant improvements in phacoemulsification equipment and in techniques are making the removal of mature lenses through small incisions safer and more reliable. One such technique is the use of green or blue dye to stain and color the capsule of the white lens intraoperatively, rendering it visible for the capsulotomy step. Another advanced surgical technique, called phaco chop, has many advantages for the mature lens nucleus. The number of US surgeons employing these newer techniques is increasing.

It is a valid dream that eventually most cataract patients in China might enjoy the remarkable benefits of small incision cataract surgery that their American counterparts now take for granted. However, there is a more pressing and immediate need - namely increasing patient access to large incision cataract surgery, the U.S. standard 15-20 years ago, in order to slow the rising tide of blindness secondary to cataract in China and throughout the rest of Asia.

A Breakthrough in Ocular Drug Delivery

Following all intraocular surgical procedures, the use of two medications - an antibiotic, and an anti-inflammatory medication (e.g. corticosteroid) - comprise the standard of care. Because intraoperative methods of drug delivery, such as periocular or intraocular injection, provide drug levels of very brief duration, topical antibiotics and steroids are prescribed postoperatively. Steroid drops are typically administered for four to six weeks.

Eyedrop medications are associated with the well know disadvantages of patient inconvenience, patient compliance issues, high cost, and significant physician and staff time spent on instruction and monitoring of topical therapy. In addition to the universal drug compliance problems of improper dosing, frequency, and confusion over different medications, topical eyedrops pose additional difficulties.

The patient must be able to get the drop into the lid cul-de-sac. Three minutes of lid closure are necessary to avoid blinking out the medication, and to minimize runoff through the nasolacrimal duct into the nasopharynx. The latter phenomenon reduces corneal drug penetration, and increases systemic absorption of the medication. Finally, topical steroids are a suspension, so patients must remember to shake the bottle, and avoid contaminating the bottle tip.

Oculex Pharmaceuticals, a biotechnology firm in Silicon Valley, has developed a unique, sustained-release intraocular drug delivery system. This tiny 1 mm pellet consists of a biodegradable polymer that is inserted into the eye at the conclusion of cataract or other intraocular surgery. Any drug, which is bound to the polymer, will be slowly released as the pellet gradually dissolves into the harmless by-products of lactic and glycolic acid. Depending on the formulation, the duration drug delivery can be programmed to occur over as short a time as several days, or over as long a period as one year. This technology

was developed by an ophthalmologist, Dr. Vernon Wong, who is ophthalmology professor emeritus at Georgetown Medical University, and co-founder of Oculex.

Their first product is a sustained release dexamethasone pellet, called Surodex, which provides a high intraocular steroid level for 7-10 days. Two clinical studies of Surodex were reported in Ophthalmology, the journal of the American Academy of Ophthalmology, in 1999. The first study was an FDA Phase II clinical trial for which I was a clinical investigator and the lead author. This prospective, randomized double masked study demonstrated Surodex to be safe and effective for post-cataract inflammation, when compared against a placebo1. For the vast majority of patients, receiving the intraocular drug delivery system eliminated the need for any topical steroid postoperatively.

The second study, by Tan, et.al. in Singapore, was a prospective, randomized, double masked study that showed Surodex to be superior at reducing inflammation in a direct comparison with topical dexamethasone2. This finding of improved efficacy may be because a much higher intraocular drug level can be obtained with this delivery system, as compared to eyedrops. Poor corneal penetration limits the amount of drug that can reach the inside of the eye via the topical route. The intraocular polymer release system bypasses the cornea and delivers drug directly to the target site. A second product that is designed to deliver a quinolone antibiotic intraocularly is being readied for human clinical trial.

While eyedrop medications pose problems of inconvenience and compliance in the U.S. patient population, the issue in China and Third World countries is one of cost and availability of postoperative medication altogether. Due to primitive operating room conditions, more traumatic surgical techniques, and increased surgical complications, far more eyes are functionally lost in Third World settings due to operative infection (endophthalmitis) and inadequately treated postoperative inflammation. Such an intraocular drug delivery system is ideally suited for this setting, particularly since there is often no follow-up of patients operated on at rural cataract camps.

Surodex has undergone a multicenter clinical trial in China, and was approved last year by the Chinese national regulatory body for use in their country. Because application for U.S. FDA approval is not expected until later this year, ironically patients in China now have access to this important breakthrough technology, while patients in the U.S. do not.

References:

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