Managing Challenges of Recalcitrant Intra-Operative Miosis during Small Incision Cataract Surgery

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Abstract. Reviewed current literature on causes and treatment of recalcitrant intraoperative miosis during small incision cataract surgery (SICS). A Medline, PubMed and Cochrane database internet search was conducted with reference manager 11. Google search was done using key words such as small incision cataract surgery and intraoperative miosis. Some pupils are inherently difficult to either dilate or sustain intraoperative mydriasis, e.g. intraoperative floppy iris syndrome (IFIS). Slow penetration through cornea, limited bioavailability and waning effects of routine topical mydriatics (TMs) are some setbacks that could pose daunting intraoperative challenges. Maintenance of sufficient pupillary dilatation during SICS can be important in successful completion of the operation. A poorly dilating pupil should be identified before surgery so that strategies and equipment are available to the SICS surgeon for the patient.

Key words: Recalcitrant, miosis, intraoperative, viscomydriasis, pupil expanders

1. INTRODUCTION

A pupil that fails to dilate beyond 4mm, often harbingered by slit lamp findings such as pseudo-exfoliation, festooned pupil from synechiae creates little access to anterior capsules during can-opener capsulotomy or rhexis. A small anterior capsulotomy or rhexis is associated with difficult nucleus manipulation en route to nucleus delivery. Several failed attempts at prolapsing the nucleus often put undue pressure on rhexis margins which already may have been compromised. Incompetent capsules of hypermature cataracts are at greatest risk of rent from forceful manipulations arising from too small anterior capsular rhexis. Other direct consequences of intraoperative miosis include vitreous loss, retained soft lens matters, high risk of iridodialysis, excessive handling of iris tissues, subsequent prostaglandin release and chronic cystoid macular edema.

1.1. THE PUPIL: physiology, drug pharmacology and transport

The pupil, bordered by a super light responsive iris, forms a passage through which aqueous egresses the posterior chamber. Pupillary aperture is not constant because of physiological hippus occasioned by autonomic control. There are 2 major types of autonomic receptors: cholinergic receptors and adrenergic receptors. The receptors of the iris sphincter are of the cholinergic muscarinic type, and the iris dilator is mainly of the α-adrenergic receptor type. While an adrenergic agent is only mydriatic, an anti-cholinergic is both mydriatic and cycloplegic. Mydriatic agents dilate the pupil by stimulating the dilator (adrenergic agonists) or by blocking the sphincter (cholinergic blockers). Adrenergic agents increase dilator activity in 3 ways: increasing norepinephrine release, interfering with norepinephrine re-uptake, and directly stimulating the α-1 receptors of the dilator, as with phenylephrine (Joel, 2011a, b).

Topical mydriatics (TMs) are applied on to the ocular surface, but the intended site of action is the iris. Only about 20% of a drop is retained in conjunctival cul-de-sac because of pre-existing volume and the rapid turnover of the tear film at 16% per minute (Cibis et al., 2003). The main penetration route for ocular pharmacological agents is through the cornea. To traverse the cornea the drug must pass through ocular barrier composed of the lipid-rich (hydrophobic) tight junctions of epithelium and endothelium (Prausnitz et al., 1998). Again, the degree of melanin pigment can affect the onset and duration of an intraocular drug. In a dark pigmented iris, the onset of dilatation is slower and the maximum pupil dilatation is limited because of melanin pigment binds the drug. Since there is a slow release from the melanin-bound drug reservoir, the effect of the drug is prolonged (De Santis and Patil, 1994). Topically
applied drops are absorbed systemically mainly through the nasal mucosa but also through the conjunctiva (Salminen, 1990; Hilary et al, 2009).

2. SOURCES OF INTRAOPERATIVE MIOSIS
(Malick and Goel, 2010; Zaczek and Zetterström, 1997)

2.1. Primary

The eye is otherwise normal. Results from ineffective dilating drop, poor administration technique, expired or fake medication (not uncommon in our African environment). Highly pigmented irides, common in Africans, dilate poorly.

2.2. Secondary

Pre-existing ocular or systemic pathology. E.g. Diabetes mellitus, pseudoexfoliation syndrome, preoperative afferent pupillary defect, anterior uveitis, pontine infarct, recent previous surgery, neurosyphilis, iridoschisis, Horner’s syndrome, synechial attachment (seclusion and occlusio pupillae), previous ocular surgery, previous laser surgery et cetera.

2.3. Trauma

Traumatic Miosis- blunt injury to the globe may rarely result in traumatic miosis and synechial formation.

2.4. Pharmacologic agents

Systemic α-1 adrenergic antagonists- e.g. tamsulosin. IFIS was reported in 2005 by John Campbell and David Chang in patients who took tamsulosin (Flomax, Boehringer-Ingelheim Pharmaceuticals, Inc., Ridgefield) for the treatment of benign prostatic hypertrophy (Chang and Campbell, 2005; Osher, 2006). It is also seen with other α-1 blockers such as doxazosin (Cardura), terazosin (Hytrin) and alfuzosin (Uroxatral). However, the frequency and severity of IFIS is apparently more severe with Flomax, perhaps because of its greater affinity for the alpha1a receptor subtype, which is present in both the prostate and the iris dilator muscle (Chang and Campbell, 2005).

Systemic tamsulosin-blocked contraction of the iris dilator smooth muscle leads to poor pupillary dilation and iris floppiness and propensity to iris prolapse. These patients also demonstrate a flaccid iris stroma that undulates and billows in response to intraocular irrigation. Only 53% of IFIS patients will have a large pupil at the outset of cataract surgery despite maximal dilating regimen. About half of these pupils will constrict during surgery (Sridhar and Davis, 2006). Other implicated medications are: chronic use of miotics e.g. topical pilocarpine, benzodiazepines e.g. diazepam and opioids e.g. morphins.

2.5. Iatrogenic

Due to excessive handling of iris intraoperatively or prolonged cataract surgery.

2.6. Age/developmental

Due to senile miosis or congenital miosis/microcoria-pupil reacts poorly to TMs due to absence/malformation of the dilator pupillae muscle or contracture of fibrous material on the pupillary margin from remnants of the tunica vasculosa lentis or neural crest cell anomalies (Toulemont et al., 1995).

3. MANAGEMENT OF INTRAOPERATIVE MIOSIS

3.1. Preoperative protocols

These comprise use of topical steroid administration at least a week before surgery in patients with anterior uveitis. Topical non-steroid anti-inflammatory drugs e.g. flurbiprofen administration at least a week before surgery or co-administered with regular dilating drops just before surgery. Cessation of miotics a week before surgery may become necessary, other classes of topical hypotensives could then be used as alternatives.

3.2. Pharmacologic techniques: topical, intracameral and viscomydriasis

Using a pharmacologic agent is the first choice for dilating the pupil. The traditional TMs are 1% tropicamide and 2.5% phenylephrine. Adjuvant non-steroidal anti-inflammatory drugs (NSAIDs) are occasionally added to TMs to enhance and sustain pupillary dilatation.
It is thought that intraocular manipulations trigger inflammatory cascade, releasing cyclooxygenase (COX) and prostaglandins within the eye causing miosis. NSAIDs inhibit COX enzymes that promote prostaglandin production; hence, providing both analgesic and anti-inflammatory activities. Studies have demonstrated topical NSAIDS (0.03% flurbiprofen (Solomon and Turkalj, 1997), 1% suprofen, 0.5% kethorolac tromethamine (Richard et al, 2011), naproxen (Papa et al, 2002), 0.5% nepafenamic (Cervantes et al, 2009) applied preoperatively can prevent intraoperative miosis. If these agents do not produce sufficient dilation, good results can often be achieved by increasing the strength or change the pharmacologic agents e.g. 10% Neo-Synephrine (Bayer Corporation, West Haven) and 2% Cyclogyl (Alcon Laboratories, Inc., Fort Worth). In some cases, patients could take the agents home and begin dilation a day ahead of surgery.

Intracameral injection of alpha-1-agonist drugs has been advocated as a means to directly stimulate the iris dilator smooth muscle receptors. Intracameral epinephrine (1:1000 bisulfite-free epinephrine mixed 1:3 or 1:4 with BSS Plus (Alcon Laboratories, Fort Worth) or plain BSS to buffer the acidic PH has been shown to be efficacious in tamsulosin-induced IFIS (Gurbaxani and Packard, 2007; Manvikar and Allen, 2006). Intracameral phenylephrine or epinephrine will dilate the pupil and in addition enhances iris rigidity by increasing dilator smooth muscle tone. This can
markedly reduce the tendency for iris prolapse and billowing. In 9% of IFIS patients with small pupils, intracameral phenylephrine can assist in a safe surgery without hooks or pupil expanders (Sridhar and Mavis, 2006).

Pupil dilatation with intracameral cocktail of 150 μl of lidocaine 1%, phenylephrine 1.5%, and cyclopentolate 0.1% has been found effective. Lidocaine obstructs the nerve conduction by blocking the sodium channels in the cell membranes, leading to an increased threshold for electrical excitability. Lidocaine can be injected into the anterior chamber of the eye and provides sufficient anaesthesia to perform cataract procedure (Gills et al, 1997). The anesthetizing effect also offers some pupil dilating capacity through its mechanism of action, i.e. to anesthetize and paralyze the muscles of the iris (Cionni et al, 2003). A solo non-preserved epinephrine (0.5ml in 500ml of Ringer’s lactate) as irrigation during surgery was found useful in a study by Vishal et al, 2011. The risk of triggering a hypertensive episode with intracameral alpha agonists is rare (Lee et al, 2007).

If the pupil still does not dilate adequately to the above pharmacologic protocols, a viscoelastic agent may be helpful (viscomydriasis). Viscosurgical devices with high molecular weights such as Healon5 (Advanced Medical Optics, Inc., Santa Ana, CA) allows for desired compartmentalization of the anterior chamber for intraocular instrumentation and working environment. It is imperative that all of the viscoelastic be removed from the eye after surgery, because residual Healon5 can cause pressure increases from trabecular meshwork obstruction.

**Fig. 7: Iris retractor**

**Fig. 8: Iris hooks**

**Fig. 9: Sinskey**

**Fig. 10: Kuglen**

### 3.3. Mechanical pupillary stretching (Howard et al, 2009; Akman et al, 2004).

If pharmacologic and viscoelastic agents are unable to dilate the pupil, iris retraction and mechanical stretching are effective options. However, the procedure can be complicated with iris sphincteric tear, bleeding, corneal touch, posterior capsule tears, ‘pseudophacodonesis’ from inadequate capsular support and vitreous loss.

**Ring expanders** cause circumferential expansion in the physiologic plane along with stabilization and protection of pupil margin. Examples are Malyugin ring system, Lester hooks, Morcher pupil dilator ring, perfect pupil, Graether 2000 pupil expander and Beehler pupil dilator. However, all of these rings are
difficult to position if the anterior chamber is shallow or the pupil is less than 4 mm wide. Therefore adjuvant viscoelastic agent should be generously used.

3.3.1. Malyugin Ring (Chang, 2008a, b). Figure 1.

It is the newest of the expansion rings developed by Boris Malyugin of Russia. The foldable one-piece square device is made of polypropylene and is much thinner than other rings, making it easier and safer to manipulate inside the eye. It has a thin profile of an IOL haptic, and so it doesn’t get in the way of instruments during surgery. Malyugin Ring is preferred to iris hooks because of easier insertion and removal, maximal pupil dilation (up to 7mm), fewer incisions (iris hooks require four additional paracenteses spaced 90° apart) and a lower risk of capsular tear.

The loading and injection system, in contrast to those for other pupil expansion rings, is disposable. This instrument is injected through main incision, thus reducing surgical trauma and minimizing the risk of contamination and postoperative inflammatory reaction. Following insertion into the anterior chamber, its four circular coils engage the pupil edge to expand it. The device catches and holds the pupillary margin steady, maximizing pupil dilation with eight touch points.

It protects the iris sphincter during surgery and allows the pupil to return to its normal shape, size and function after the operation. Because of how the iris drapes over it, the Malyugin ring, in contrast to iris retractors, creates a rounded rather than a square pupillary opening. Being atraumatic, it is particularly useful in patients for whom cutting or tearing of the iris tissue should be avoided, especially in the presence of rubeosis, chronic anterior uveitis or systemic coagulopathy. Most importantly, it creates sufficient anterior segment working environment for instrumentation.

3.3.2. Lester Hooks

(Katena Products Inc., Denville). One hook is inserted through the main incision, and the second hook is inserted through the side port. The hooks engage the pupillary margin at opposite points. They are then pulled apart, moved 90°, and pulled again to manually dilate the pupil. Alternatively, polypropylene iris hooks (Grieshaber, Schaffhausen, Switzerland) can be placed through paracenteses and used to expand the pupil; they are kept in place until after continuous curvilinear capsulorrhexis (CCC) and lens implantations are completed (Oetting and Omphroy, 2002). See figure 2.

3.3.3. Morcher pupil dilator

Shown in figure 3; Occasionally, the iris is stretched but the pupil will not dilate, a Morcher pupil dilator (Morcher GmbH, Stuttgart, Germany) may be helpful. It is a poly methyl metacrylate ring placed at the pupillary margin that uniformly expands the pupil through 300°. In cases of IFIS, it prevents prolapsing of floppy iris. The ring is inserted through the main incision using hooks. The central segment of the ring is manipulated in opposition to the distal pupillary margin and its ends placed with the aid of its eyelets. Following IOL implantation, the ring is removed by freeing its ends from their point of apposition with the pupil by means of a small hook, again placed in each eyelet. Finally, the ring is withdrawn from the A/C with a forceps. Morcher dilator and Perfect pupil are prototypes of pupil rings (Kershner, 2002).

3.3.4. Milvella Perfect Pupil; Figure 4.

It was developed in the 1990s by John E. Milverton. Like Morcher, it is a pupil ring. However, it is made of a sterile polyurethane device that features a safety arm that sticks out of the incision and prevents it from becoming lost in the eye. When placed insitu, it enlarges the pupil to a circle approximately 8 mm in diameter, protecting the pupil margin during surgery. A new injector system akin to IOL injector makes it suitable in all incision types; clear cornea, scleral and limbal. Capsulorrhexis, hydrodissection, and IOL insertion can all be safely carried out with the perfect pupil expansion ring (Milvella Pty Ltd, Epping, Australia) in place.

3.3.5. Graether (Gaether, 1996) Shown in figure 5.

The Graether Pupil Expander (Eagle Vision, Inc, Memphis) is particularly useful for countering the iris-related abnormalities induced by Flomax. It is a soft silicone ring grooved to engage the iris sphincter and maintain pupil dilation. When expanded, the inside diameter of the ring is 6.3mm. It is preloaded onto a disposable plastic injector to allow for insertion through the primary surgical incision.

3.3.6. The Beehler Pupil Dilator (Moria, Antony, France), see figure 6.

This pupil dilator comes either two- or three-pronged. In both designs, one hook wraps around the sub-incisional pupillary margin. The surgeon then pushes a plunger, and either two or three prongs emerge from the tip. The prongs feature small hooks that engage the distal pupillary margin. In one motion, the whole pupil is dilated. Because the Beehler pupil dilator
creates more uniform dilation by distributing tension on all sides of the pupil, eyes will frequently have a better cosmetic appearance postoperatively than after the use of two Lester hooks. The proximal hook, which goes under the sub-incisional pupillary margin, should be introduced and removed in a sideways fashion to avoid ragged tear to the inner lip of the incision. Undue downward pressure on the lens while mechanically dilating the pupil should be avoided, especially in eyes with pseudo-exfoliative syndrome associated with weak zonules.

3.3.7. Iris Retractors, figure 7.

Four side ports, through each of which a retractor is inserted, create a square dilated pupil. However, anterior chamber may not form because of fluid egresses out of the eye from the multiple paracenteses. This compromised ocular fluidics makes Iris retractors unpopular.

3.4. Other Mechanical Pupil Expansion Devices- iris hook (Mackool, 1992), Sinskey, and Kuglen. Figures 8, 9 and 10 respectively.

3.4.1. Synechiolysis

If posterior synechiae are present, viscomydriasis can be augmented with synechiolysis using iris spatula to sweep under the iris.

3.4.2. Surgical techniques: pupilloplasty, sphincterectomies, wound geometry

Pupilloplasty- Although most surgical techniques for expanding the pupil have fallen into disuse because of the development of the aforementioned instruments, pupillary membrane dissection is sometimes still necessary. Pupilloplasty (Osher, 1991) can be carried out for fibrotic membrane around the pupillary margin that can prevent dilatation.

Mini sphincterectomies- this can be performed with long vannas’s scissors through the main wound or side port. Sphincterectomies should be done one at a time depending on the need to have more. Cuts should not go beyond the pupillary sphincter.

Wound geometry- In IFIS, paying a careful attention to incision construction has been advised.

4. POSTOPERATIVE CONCERNS

Postoperatively the pupil may fail to constrict despite stroke the pupil with a hook or spatula during surgery. Intraoperative Miochol-E (Novartis Ophthalmics, Inc., Duluth, GA) and postoperative pilocarpine instillations can constrict the pupil.

5. CONCLUSION

Adequate transpupillary access to the cataractous lens is essential for the success of SICS especially in cases with zonular weakness and capsular inadequacy. The availability of many devices has provided therapeutic options that reduce complications of small pupils during SICS. The other important factor is sufficient manipulability of the instruments, which is critical for the successful completion of surgery.

REFERENCES


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