ABSTRACT: Pseudoexfoliation syndrome is characterised by the production and progressive accumulation of fibrillar extracellular material within different ocular tissues, and its incidence varies considerably according to geographical location. Cataract surgery in pseudoexfoliative patients is associated with a higher rate of complications, which are more common the more advanced the cataract. For this reason, the approach in these cases requires a thorough pre-operative study, a carefully planned surgical strategy and appropriate post-operative follow-up, which are the issues discussed in this review.


First described in 1917 by Lindberg¹, pseudoexfoliation syndrome is an age-related disease characterised by the production and progressive accumulation of fibrillar extracellular material within different ocular tissues. According to epidemiologic studies², it is responsible for 20–25% of open-angle glaucoma, representing the most common known cause worldwide.

There is an association between pseudoexfoliation and cataracts, possibly due to ocular ischemia and defective antioxidant defence mechanisms³. Moreover, cataracts appear sooner and progress quicker in these patients⁴. Like cataracts, the incidence of pseudoexfoliation increases with age⁵; in the USA, the rate was found to increase from 0.6% at 65 years to 5% from 70 years on⁶.

Cataract surgery in pseudoexfoliative patients has always been associated with a greater number of complications, for some authors⁷-⁸ even up to 5 and 10 times greater. However, with new advances, more recent studies have shown this figure to be between 1.5 and 3%⁹,¹⁰, depending on the level of severity and progression of the pseudoexfoliation, which takes us to the first important consideration: Cataract surgery must be performed earlier than in routine cases.

Why is it a challenging surgery?
Mainly because there are two very significant risk factors:
1. Poor pupillary dilation due to the iris ischemia that accompanies the syndrome, as well as the infiltration of extracellular material into the iris, which produces a mechanical obstruction to dilation¹² (Figure 1).
2. Progressive zonular weakness that increases in hard cataracts, old age, glaucoma and poor pupillary dilation (Figure 2).

Surgical considerations
Naturally, the difficulty of the surgery will depend on pupil dilation, hardness of the nuclei, but also, and to a greater extent, on zonular weakness, which is why we can find pseudoexfoliative patients for whom surgery is very straightforward and others for whom it is extremely difficult, especially with very hard cataracts, significant zonular weakness and poor pupillary dilation (Figure 2).

---

¹Department of Ophthalmology, Complejo Hospitalario Universitario Orense, Orense, Spain
²Department of Ophthalmology, Complejo Hospitalario Universitario A Coruña, A Coruña, Spain
³Centro de Oftalmología Barraquer, Barcelona, Spain

Financial Disclosure: The authors do not have any financial interest in any of the products mentioned

Corresponding Author: Dr Ramón Lorente Moore C/ Calle del Paseo, 19-2ª, 32003, Orense, Spain, E-mail: rlorenteofal@yahoo.es
Direct instability signs are:

- **Phacodonesis**, better perceived without dilating the pupil, or even with a drop of pilocarpine 2%\(^1\), which relaxes the zonule and facilitates lens movement.

- **Iridodonesis**.

- **Subluxation** which always starts in the superior area\(^1\).

Some of the indirect signs we must look for are significant changes in the depth of the chamber, whether it is very narrow or deep, especially if it is asymmetric (Figure 3). Likewise, a mature cataract, glaucoma and old age are considered indirect signs of potential zonular instability.

Cataract surgery in pseudoexfoliative patients has special requirements as follows:

a) Detailed Pre-operative study.

b) Carefully Planned surgical strategy.

c) Closer Post-operative follow-up.

a) **Detailed Pre-operative study.** Its aim is to avoid as many intra-operative surprises as possible and to choose a surgical plan.

First of all, we have to assess potential glaucoma and the status of the optic nerve, perform a dilation test with the same drops to be used in the operating theatre to gauge the level of dilation exactly, and to determine if any mechanical method will be required to achieve adequate dilation.

Perhaps the most important study is to assess if there are signs of zonular instability.
b) Carefully Planned surgical strategy. There is no doubt that each eye is different, and depending on the previous examination, the surgical plan will differ in some way, although some basic aspects that are used with all patients have to be taken into account:

Dilation
For patient dilation, we use topical tropicamide 1%, phenylephrine 10% and non-steroid anti-inflammatory drugs (NSAIDs) 4 times starting 1 hour before surgery. In those patients who do not dilate enough with this regimen, we apply an intracameral injection of lidocaine and adrenaline at the beginning of surgery, although this has had little success.

Anaesthesia
The type of anaesthesia depends on the surgeon’s experience and on any potential complications that we can expect. Topical anaesthesia is recommended. If peribulbar or sub-Tenon’s is used, it is better to inject a small amount and to place the Honan balloon with less pressure to avoid damaging the zonule.

Incision
It is advisable to perform the incision through a temporal approach, since as we have already said, the zonular instability begins in the superior area and it is more traumatic for the zonule to work in the area where the potential zonular alteration is located.

Ophthalmic viscosurgical devices (OVD)
We need to use an OVD which, in addition to protecting the endothelium, lasts during the entire process; it is also recommended not to hyper-pressurise the anterior chamber in order to avoid further zonular damage. A good option is the soft-shell technique, which combines the use of two OVDs: a cohesive and a dispersive one (Figure 4).

Figure 4. Arshinoff’s soft shell technique of OVD application.
Pupillary manoeuvres

In our experience, pharmacological methods such as intracameral adrenaline or phenylephrine are not effective as they do not increase the previous topical dilation, so we have to resort to mechanical methods: stretching (which is our first choice), iris retractors, Malyugin ring, Beehler pupil dilator, dilation ring, and even micro, which in many cases can get us out of a problem (Figure 5).

It is important to remember that all these methods produce an alteration in the blood-aqueous barrier, already affected in these patients, with a subsequent increase in post-surgical inflammation. In previous studies, it was concluded that all procedures were effective in dilating the pupil, and similarly, all of them caused trauma to the iris, although somewhat less with the dilation ring. Due to these adverse reactions, we believe that as long as we can operate safely, it is advisable not to alter the pupil.

Capsulorhexis

A 5-6 mm capsulorhexis should be performed. If we cannot achieve this size due to pupil miosis, it is advisable to try to increase it at the end of surgery. If this is not possible it is important to perform a YAG laser relaxing capsulotomy in the immediate postoperative period (within the first month).

In those cases in which we have to stain the anterior capsule to improve its visualisation, the use the sweeping technique is recommended: we inject a few drops of trypan blue under the OVD and spread it on the anterior capsule with a spatula (Figure 6). In this way, we prevent the dye from getting into the vitreous cavity through an impaired area, which would make the surgery considerably more difficult.

Hydrodissection

This is a mandatory step to isolate the nucleus of the cortex and the capsular bag, thus minimising zonular damage during phacoemulsification.

First of all, we must remove some of the OVD to avoid excessive pressure in the anterior chamber, which may complicate the manoeuvre; this simply requires the lower lip of the incision to be depressed with a cannula.

Hydrodissection should be performed in all quadrants, as described by Vasavada: i.e. the injection of (BSS) in 3 or 4 areas so that stress is distributed throughout the bag. We must remember that the hydrodissection is not finished until we see the BSS flowing out of the capsular bag.

If we want to implant a capsular ring before phacoemulsification, it is desirable to perform the hydrodissection with a cohesive OVD to create a wider intrasacular space.

Before starting phacoemulsification, it is important to ensure that the nucleus rotates freely in the capsular bag; sometimes zonular weakness can make this rotation difficult, and we have to do it bimanually as it makes it easier and safer, with a collar button spatula through the main incision and a chopper or similar through the paracentesis (Figure 7).
Phacoemulsification Technique

Certainly, this will depend on the hardness of the cataract. In soft cataracts it is more advisable to use a "divide and conquer" flip and chip technique, always taking care not to "push" the nucleus.

The problem is greater in hard cataracts, where the vertical chop produces less traction on the zonule. It has another advantage, especially in small pupils, which is that we always see the chopper and the tip of the phacoemulsifier as we work in the centre of the pupil, which does not occur in the horizontal chop (Figure 8). Recently, we have been working on very hard cataracts using Escal's ultrachopper, and we have the impression that the division of the nucleus is less traumatic than with chop techniques (Figure 9).

Regardless of the technique we use, there are a series of important considerations during phacoemulsification so as not to increase zonular weakness:

- Use parameters that do not create chamber fluctuations.
- Always introduce the tip of the phacoemulsifier with the irrigation bottle in a low position and raise it slowly to the appropriate height. With these manoeuvres we reduce zonular stress as well as the risk of fluid misdirection syndrome.
- Use low flow and vacuum settings – slow motion phacoemulsification –.
- Modulate the ultrasound energy.
- Avoid anterior chamber collapse when removing the instruments; sometimes it is necessary to inject viscoelastic through the paracentesis before.

Capsular ring

It is an essential device in pseudoexfoliative patients. Its function is to distribute traction through the zonule, avoiding its concentration in only one place.

It is only valid in small subluxations less than 4 hours in extent, and although it provides stability in the zonule, it does not always prevent an increase in the subluxation. Likewise, it does not prevent either postoperative capsular contraction or potential late in-the-bag intraocular lens dislocation.
There is some controversy over which is the most appropriate time to implant the ring: before phacoemulsification or upon completion of irrigation/aspiration (I/A) (Figure 10).

At first it might seem that it is better to implant it before the phacoemulsification, but according to studies by Ahmed, Cionni and Crandall, this would create non-desirable effects such as: an increase in the displacement of the capsular bag, an increase in the elongation and zonular tension and more difficult surgery, especially the aspiration of cortical masses. If it is implanted beforehand, Vasavada recommends viscodissection instead of hydrodissection to create space.

Implanting the ring after the I/A facilitates the surgery but may be too late.

We prefer to implant the ring when we observe an increase in zonular instability, independently of the phase of the surgery, but we do not implant it systematically before phacoemulsification.

There are various signs that may lead us to suspect an increase in instability during phacoemulsification: increased difficulty in rotating the nucleus or fragments, visualisation of the subluxation area, ovalisation and flaccidity of the edge of the rhexis (Figure 11), presence of vitreous with subsequent loss of ultrasound efficiency, or if we can see the capsular fornix when retracting the cortex.

We can summarise all of the above in one sentence: “Implant the ring as late as you can and as soon as you must”.

The ring must always be implanted starting in the direction of maximum instability so as not to increase it. It is also advisable to suture a thread at its end, which does not get in the way during the surgery. If instability increases it facilitates the removal of the device.

When subluxation is larger than 4 hours, rings are not effective and we must use capsular retractors to hold the capsule during phacoemulsification, before suturing it to the sclera using a Cionni ring or an Ahmed segment (Figure 12).

Mackool retractors (MackoolTM Cataract Support System; FCI Ophthalmics) Marshfield Hills, MA, USA are the most commonly used, although I believe those from MST (UUMicroSurgical Technology; Redmond, WA, USA) are more efficient and less traumatic for the rhexis. Another possibility is to use iris retractors, although they tear the rhexis more easily.

Irrigation/Aspiration

The period of higher risk is probably when there is abundant cortex and poor pupil dilation, as there is greater zonular traction when it is aspirated. In order to produce less stress in the zonule, we have to aspirate the cortex with tangential movements. If it is too adhered to the capsular bag or to the capsular ring (if we have implanted one), hydrating it makes it easier to extract. It is also useful to use an undulated Henderson ring, although it may not be as effective as more rigid rings for other purposes.

Likewise, the bimanual technique makes this surgical step easier, as we can access the full 360° of the capsule.

Anterior capsule polishing

This must be done to minimize the contraction of the anterior capsule; the central 6 mm are removed by aspiration, as this is the area that covers the lens optic and where the highest concentration of “A” crystalline cells with contractile ability is located. It is recommended not to aspirate the rest of the capsule to allow for capsular fusion, and to avoid the migration of the equatorial cells into the centre of the posterior capsule (Figure 13).
Intraocular lens

It is important to implant a lens with the greatest biocompatibility (hydrophobic acrylic) to reduce potential inflammation, with squared edges to reduce posterior capsule opacity, with slow unfolding in the anterior chamber and through a properly sized incision (Figure 14).

After intracameral injection of the preferred antibiotic (in our case moxifloxacin), we combine hydrocortisone to minimise post-surgical inflammation.

c) Closer Post-operative follow-up. - This is more insidious and requires closer follow-up due to increased potential complications, which can be divided into early and late.

Among the early complications are:
- Inflammation due to the rupture of the blood-aqueous barrier, which will increase depending on the extent of the trauma to the iris.
- Presence of synechia.
- Pressure spikes; A study by Shingleton showed pressure over 30 mmHg in 7% of patients, reaching 17% in previously glaucomatous patients.
- Likewise, these patients are predisposed to corneal oedema, as pseudoexfoliation has endothelial alterations that favour their onset.
- Capsular contraction is another early complication that can lead to a cascade of complications if left untreated. We know that contraction occurs within the first month, so we must monitor it, dilating the patient around week 3. If there is contraction, 4–5 YAG laser relaxing capsulotomies should be performed at the edge of the rhexis, an easy and effective maneuver (Figure 15).

The greater the inflammation, the greater the contraction and zonular weakness. This is not related to the previous size of the rhexis; the main risk factor for capsular contraction is inflammation. Capsular
shrinkage not only causes lens displacement, it also leads to progressive weakening of the zonule.

Late complications include the following:
- The most important is late spontaneous in-the-bag intraocular lens dislocation. This is due to progressive zonulopathy associated with capsulorhexis and pseudoexfoliation (Figure 16). According to a study carried out in 45 patients, the timeframe for onset is 7 years. The capsular ring does not prevent dislocation, and it is important to secure the haptic or ring to the sclera at the first sign of pseudophacodonesis. In advanced cases, there is no alternative but to remove the entire complex and perform a secondary implant.
- Posterior capsular opacification—The incidence is higher in these patients, due to their greater postoperative inflammation and greater difficulty in cleaning the capsular bag thoroughly.

Figure 16. Late in-the-bag intraocular lens dislocation. A) Eight years after surgery; B) Repositioning of the IOL-bag complex by means of ab externo scleral fixation.

CONCLUSION

Cataract surgery in pseudoexfoliation patients remains a challenge for surgeons, especially in cases with zonular instability and advanced cataract.

In order to improve results, we must perform a rigorous preoperative study, customise the surgery aiming to stabilize the capsular bag as much as possible, and carry out a more exhaustive postoperative monitoring.

REFERENCES

1. Lindberg JG. [Clinical studies of depigmentation of the papillary margin and transillumination of the iris in cases of senile cataract and also in the normal eyes of the aged]. Thesis. Helsinki, Finland, Helsinki University 1917.


