Original article

Posterior capsule opacification, capsular bag distension syndrome, and anterior capsular phimosis: A retrospective cohort study

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ABSTRACT

Objective: To determine the incidence and the risk factors involved in the development of the three main postoperative capsular complications: posterior capsule opacification (PCO), capsular bag distension syndrome (CBDS), and anterior capsular phimosis syndrome (ACP).

Subjects, materials and methods: A retrospective cohort study was conducted on 801 patients submitted to cataract surgery in the ophthalmology unit of Hospital del Henares (Madrid) from March 2, 2009 to February 28, 2010. Computerized clinical charts were reviewed during July 2012. PCO was studied using the Kaplan–Meier method (log rank test).

Results: A total of 167 patients developed PCO. No association could be demonstrated between PCO and age, sex, diabetes mellitus, phaco technique, IOL model, tamsulosin intake, glaucoma, and age-related macular degeneration. Three patients developed CBDS, all of them had received a Akreos Adapt AO® (Bausch & Lomb). Two of them were young men who had received surgery for posterior subcapsular cataracts. Three patients developed ACP, 2 of whom had received a MicroSlim® IOL (PhysIOL).

Conclusions: No association was found between PCO and any of the studied variables. Male gender, young age, subcapsular cataract and large non-angulated lens such as Akreos Adapt AO® could be associated with CBDS. ACP could be more frequent when microincision IOLs (like MicroSlim®) are implanted.

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Opacificación de la cápsula posterior, síndrome de distensión capsular y síndrome de fimosis de la cápsula anterior: estudio de cohortes retrospectivo

RESUMEN

Palabras clave:
Opacificación de cápsula posterior
Síndrome de distensión capsular
Fimosis de la cápsula anterior
Capsulotomía Nd–YAG
Complicaciones de cirugía de catarata

Objetivo: Determinar la incidencia y los factores de riesgo implicados en el desarrollo de las tres principales complicaciones capsulares postoperatorias: opacificación de cápsula posterior (OCP), síndrome de distensión capsular (SDC) y fimosis de la cápsula anterior (FCA).

Sujetos, material y métodos: Estudio de cohortes retrospectivo. Se incluyó a 801 pacientes operados mediante cirugía de catarata en el Servicio de Oftalmología del Hospital del Henares (Madrid), entre el 2 de marzo de 2009 y el 28 de febrero de 2010. La historia clínica electrónica fue revisada durante el mes de julio de 2012. La OCP se estudió utilizando el método de Kaplan–Meier (log rank test).

Resultados: Un total de 167 pacientes desarrollaron OCP. No se pudo demostrar asociación entre la OCP y edad, sexo, diabetes mellitus, técnica de facoemulsificación, modelo de lente intraocular (LIO), consumo de tamsulosina, grado de síndrome de iris flácido intraoperatorio, glaucoma ni la degeneración macular asociada a la edad. Tres pacientes desarrollaron SDC, todos ellos habían recibido una LIO Akreos Adapt AO® (Bausch & Lomb). Dos de ellos eran varones jóvenes, con diagnóstico de catarata subcapsular posterior. Tres pacientes desarrollaron FCA, dos de ellos habían recibido una LIO MicroSlim® (PhysIOL).

Conclusiones: No pudo demostrarse asociación de la OCP con ninguna de las variables estudiadas. El sexo masculino, la edad joven, la catarata subcapsular posterior y las LIO grandes no anguladas como la Akreos Adapt AO® podrían asociarse al desarrollo de SDC. Las LIO de microincisión, como la MicroSlim®, podrían asociarse al desarrollo de FCA.

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Introduction

Posterior capsule opacification (PCO) is the most frequent complication in cataract surgery. In developed countries it can be safely treated utilizing neodymium–doped yttrium aluminum garnet laser (Nd–YAG). However, treatments for this complication involve significant costs. In developing countries where laser technology is not readily available, PCO continues to be an important cause of severe visual loss, requiring ophthalmologists to adopt imaginative solutions.

PCO is the consequence of the ability of the lens to regenerate on the basis of epithelial residual cells. Even though our knowledge of the natural history of this complication has improved in recent years, many details still remain to be discovered. The literature discussing risk factors involved in PCO is contradictory, to the point that a recent Cochrane Collaboration review has concluded that only the design of the intraocular lens (IOL), small diameter capsulorhexis and implantation inside the capsular bag reduce the incidence of this complication.

The capsular bag distention syndrome (CDS) and anterior capsular phimosis (ACP) are less frequent complications with very few cases reported in the literature. In fact, many publications refer only one or 2 cases, frequently omitting important information such as the type of cataract exhibited by the patient or the model of implanted IOL. The authors believe this is the first cohort study analyzing the aggregate incidence and risk factors involved in the development of said 3 complications concurrently.

Subjects, materials and methods

Between March 2, 2009 and February 28, 2010, 801 cataract operations were performed at the Ophthalmology Service of the Henares University Hospital (Coslada, Madrid). Said hospital is a secondary center covering an area with about 190,000 inhabitants. The Ophthalmology Service comprises 8 ophthalmologists who perform about 100 cataract operations every year. The electronic clinic history of patients was reviewed by JCMM in the course of July, 2012.

All the patients were administered presurgery prophylaxis with topical ofloxacin during 3 days and were dilated by means of 3 drops of tropicamide (Coliruc Tropicamida®, Alcon Labs, Fort Worth, TX, USA), and a further 3 of phenylephrine (Colirucsi Fenilefrina®, Alcon Labs). Two different phacoemulsification devices were used, i.e., Infiniti® (Alcon Labs) and Stellaris® (Bausch & Lomb, Rochester, New York, USA). Three types of IOL were implanted: Akreos Adapt AO® (Bausch & Lomb); Acrysof IQ SN60WF® (Alcon Labs) and MicroSIM® (Physiol, Liege, Belgium). In all cases the cataracts were operated by means of an incision in the clear cornea, usually under topical anesthesia. Intracameral 1% lidocaine was systematically injected in the anterior chamber at the beginning of the intervention and 1 mg cefuroxime at the end thereof. If the
Table 1 – Patient characteristics patients.

<table>
<thead>
<tr>
<th></th>
<th>No complications capsulotomies</th>
<th>PCO</th>
<th>ACP</th>
<th>CDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. (eyes)</td>
<td>628</td>
<td>167</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>72.6 (SD = 9.3)</td>
<td>71.6 (SD = 8.6)</td>
<td>73 (SD = 0)</td>
<td>62.7 (SD = 12.2)</td>
</tr>
<tr>
<td>Nuclear cataract grade median (LOCS III)</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>HTA %</td>
<td>46.2</td>
<td>51.2</td>
<td>33.3</td>
<td>0</td>
</tr>
<tr>
<td>Diabetes mellitus %</td>
<td>21</td>
<td>18.1</td>
<td>0</td>
<td>33.3</td>
</tr>
<tr>
<td>Glaucoma or ocular hypertension %</td>
<td>9.7</td>
<td>11.4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>ARMD %</td>
<td>7.4</td>
<td>10</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Follow-up: median (range) (months)</td>
<td>16.6 (0–38.9)</td>
<td>22.7 (1–39.7)</td>
<td>5.9 (3–18.5)</td>
<td>23.8 (16.7–36)</td>
</tr>
<tr>
<td>Mean axial length (mm)</td>
<td>23.2 (SD = 1.2)</td>
<td>23.4 (SD = 1.5)</td>
<td>23 (SD = 0.6)</td>
<td>23.5 (SD = 1.1)</td>
</tr>
<tr>
<td>Mean AC depth (mm)</td>
<td>3.1 (SD = 0.4)</td>
<td>3 (SD = 0.4)</td>
<td>–</td>
<td>3.5 (SD = 0.7)</td>
</tr>
<tr>
<td>Power of implanted IOL (diopters)</td>
<td>20.8 (SD = 3.3)</td>
<td>20.3 (SD = 4.1)</td>
<td>22.2 (SD = 1.8)</td>
<td>20.8 (SD = 2.9)</td>
</tr>
</tbody>
</table>

Implanted IOL (%)

<table>
<thead>
<tr>
<th></th>
<th>Akreos Adapt AO</th>
<th>Physiol Microslim</th>
<th>Acrysof IQ</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. (eyes)</td>
<td>467 (74.4)</td>
<td>138 (82.6)</td>
<td>9 (5.4)</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>62.1 (SD = 6.7)</td>
<td>64.8 (SD = 6.2)</td>
<td>63 (SD = 6.5)</td>
</tr>
<tr>
<td>Nuclear cataract grade median (LOCS III)</td>
<td>3.5</td>
<td>4.0</td>
<td>2.8</td>
</tr>
<tr>
<td>HTA %</td>
<td>52.7</td>
<td>53.2</td>
<td>51.6</td>
</tr>
<tr>
<td>Diabetes mellitus %</td>
<td>22.3</td>
<td>20.2</td>
<td>24.5</td>
</tr>
<tr>
<td>Glaucoma or ocular hypertension %</td>
<td>8.7</td>
<td>10.2</td>
<td>13.5</td>
</tr>
<tr>
<td>ARMD %</td>
<td>6.7</td>
<td>7.6</td>
<td>6.2</td>
</tr>
<tr>
<td>Follow-up: median (range) (months)</td>
<td>16.6 (0–38.9)</td>
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<td>22.2 (SD = 1.8)</td>
</tr>
</tbody>
</table>

Results

Overall, 801 cataracts of 656 patients were operated on between March 2, 2009 and February 28, 2010. Of said eyes, 380 (47.4%) were of male patients. The medical and demographic characteristics of the sample are summarized in Table 1. The mean age of patients was 72.9 years (standard deviation: 9.1 years). The mean cataract grade was 3 (LOCS III classification).

The majority of patients were treated with “conventional” phacoemulsification through 2.75 mm (548 eyes), while the remaining 253 eyes were treated with microincision surgery through a 2 mm insertion. Three different IOL were implanted: Akreos Adapt AO® in 609 eyes (76%); Acrysof IQ SN60WF® in 55 eyes (7%) and MicroSlim® in 137 eyes (17%). Three eyes received anti-VEGF injection combined with cataract surgery.

After 3 years follow-up, 167 eyes developed PCO, while 3 eyes were diagnosed with CDS and a further 3 with ACP. Utilizing the Kaplan–Meier method, no association could be demonstrated between PCO and any of the studied variables (Table 2). The statistical significance level was adjusted to 0.006 because it 9 comparisons were carried out, i.e., use of tamsulosin (log rank test p = 0.713); intra-surgery floppy iris syndrome grade (log rank test p = 0.913); IOL model (log rank test p = 0.532); diabetes mellitus (log rank test p = 0.467); glaucoma (log rank test p = 0.966); ARMD (log rank test p = 0.795); phacoemulsification technique through 2.75 mm vs 2 mm (log rank test p = 0.142); sex (log rank test p = 0.018). In addition, using Cox regression no relationship with age could be demonstrated (p = 0.466).

During the period of time comprised by the study, only 3 eyes developed capsulotomy-related complications from the Bioethics Committee. Data were stored in an Excel database and subsequently transferred to SPSS 15.0 for Windows (SPSS Inc., Chicago, IL, USA) for statistical analysis. The statistical significance record was established at 5% (p < 0.05). When multiple comparisons were carried out the significance threshold was adjusted using the Bonferroni correction.
Table 2 – Influence of studied variables in posterior capsule opacification. Adjusting significance by the number of comparisons, none reached significance.

<table>
<thead>
<tr>
<th>Variables</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use of tamsulosin</td>
<td>0.713a</td>
</tr>
<tr>
<td>Intra-surgery floppy iris syndrome</td>
<td>0.913</td>
</tr>
<tr>
<td>IOL model</td>
<td>0.532a</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>0.467a</td>
</tr>
<tr>
<td>Glaucoma</td>
<td>0.966a</td>
</tr>
<tr>
<td>ARMD</td>
<td>0.795a</td>
</tr>
<tr>
<td>Phacoemulsification (2.75 vs 2 mm)</td>
<td>0.142a</td>
</tr>
<tr>
<td>Sex</td>
<td>0.018</td>
</tr>
<tr>
<td>Age</td>
<td>0.466d</td>
</tr>
</tbody>
</table>

* Log rank test.

b Cox regression.

(2 eyes exhibited “pitting” in IOL, and one suffered a retinal detachment months after receiving the laser treatment). None of the complications were detected in the scheduled visit one month after the capsulotomy.

Discussion

Posterior capsule opacification

PCO is the most frequent complication in cataract surgeries. It has a negative impact not only on visual acuity but also on other visual functions such as contrast sensitivity or even stereo visual acuity in addition to producing glare as demonstrated by simulation studies carried out by van Bree et al. For these reasons, PCO reduces quality of life in addition to interfering with ocular fundus examinations and other diagnostic procedures such as optic coherence tomography. Even though laser technology enables quick and safe treatment of this complication, the fact remains that said treatment is resource consuming. In less developed countries where laser technology is not readily available, PCO constitutes a severe problem which threatens the eyesight of patients sometimes only months after being operated for cataracts. In addition, population aging and the increasingly earlier indication of cataract surgery, together with higher patient expectations, are likely to increase the significance of this complication in the next few years. Intra-surgery chemophrophylaxis of this complication has been tested with some success in experiment animals, but at present the endothelial toxicity of available drugs restricts the use of this measure in clinical practice. In this regard it would be interesting to determine the effect of anti-VEGF drugs on PCO as it has not been very well documented. However, in our series it was not possible to assess this aspect because one of these drugs was administered concurrently in only 3 eyes.

Accordingly, in-depth knowledge of said complication is of vital importance, as attested by hundreds of reports being published every year on the topic. However, the literature on related risk factors is surprisingly inconsistent despite its abundance. By way of example, some authors consider diabetes mellitus to be a risk factor while others consider it a protective factor. It is likely that a large amount of reports such as this one (which did not find associations in any of the 2 options) may never be widely disseminated due to several factors, one of them being that the studies involve different populations and use different methodologies, in addition to the fact that many are case–control studies where the adequate selection of controls is of vital importance.

A further 2 capsular complications have been reported in the literature, although with lesser frequency: CDS and ACP. Most part of the reports discussing these 2 complications comprises small series focused on a handful of cases. The authors believe this is the first paper studying the 3 complications simultaneously from the perspective of a cohort study.

In the present study, the aggregate incidence of PCO during the study period was 21%, similar to the percentages published in other series. The present sample is not the best one for studying the influence of IOL in PCO, because most of the patients were implanted with an Akreos Adapt AO IOL. In all cases, the survival curve of the 3 IOL types was very similar (log rank test $p = 0.532$).

Said results contradict some previous publications associating acrylic IOL to a lower PCO incidence but match the results of other papers which consider that a straight edge is the key factor for preventing this complication regardless of the material. In fact, the most recent systematic review concluded that the material has no influence and the truncated edge is the only IOL-dependent protective factor.

Some studies have found greater incidence of PCO in diabetic patients while others conclude exactly the opposite. In the present sample, diabetic as well as nondiabetic patients developed this complication with very similar incidence rates. Some factors could influence the decision of performing capsulotomy in these patients; on the one hand, concern about worsening macular edema could delay the operation, while on the other the need to explore the retina or treating it with laser could lead to the decision of carrying it out earlier.

In what concerns gender influence, the situation is similar. Some studies have found similar incidence rates in males while others have found higher rates in females. In the present sample, PCO was more frequent in females ($p = 0.018$) but, after adjusting the significance level for multiple comparisons, said difference was not significant.

The authors have observed that most of the published studies assessed concurrently the influence of several variables without adjusting the significance level according to the number of comparisons carried out, and this could easily lead to the appearance of false positives. In fact, if the Bonferroni correction had not been applied in the present sample, the probably spurious conclusion that PCO is more frequent in females would have been reached.

There is no consensus about whether or not patients should follow routine examinations after laser treatments. A survey carried out among British ophthalmologists demonstrated considerable variability in the way capsulotomy is carried out. Overall, 60% do not examine the patient while the remaining 40% consider examinations a recommendable practice. The data of the present study indicate that a review is not necessary as complications are very infrequent and none were detected or prevented by scheduled visits. Accordingly, since 2011 patients are not reviewed by the authors.
**Capsular distention syndrome**

The present cohort includes 3 patients that developed belated CDS. All were males, intervened for cataract surgery without complications and had been implanted with Akreos Adapt AO® IOL. It is worth noting that 2 of the said patients were young males who had been operated on the same day (Table 1). Two of these exhibited cataracts with a significant posterior subcapsular component. The group of patients that developed this complication was 10 years younger than those who did not develop it.

From the chronological viewpoint, CDS can be classified as intra- or post-surgery. The intra-surgery form has been described in relation to the generation of gas during femtosecond laser-assisted cataract surgery. Within the post-surgery forms, the early ones are probably due to the retention of viscoelastic or cortical material behind the IOL while the late forms are probably produced by the proliferation and metaplasia of epithelial cells. These cells produce collagen and other extracellular matrix materials which accumulate in the capsular bag. In fact, electrophoresis of sequestered material confirmed the presence of large amounts of alpha-crystalline protein, which indicates that the material is derived from residual epithelial cells.

The present series does not include any patient with early CDS. As the pupil does not systematically dilate in the first post-surgery visit, the likelihood of most of these cases remaining undiagnosed is high. In fact, Pinarci et al. consider that said syndrome can be a casual finding on many occasions and that patients frequently remain undiagnosed until they subsequently develop PCO.

Even though CDS pathogenicity is not very well understood, some risk factors have been associated with this complication. Virtually all IOL models have been related with this complication, including accommodative or multifocal IOL varieties. In the present cohort, all the cases emerged in patients who had received Akreos Adapt AO® IOL. Considering that CDS is a very infrequent complication and that this model was used the most, said association cannot be confirmed. However, in other relatively recent cohort studies, 6 of 8 cases appeared in patients who had received said IOL (although in said study only 19% of patients had been implanted with this model). The large surface of this haptics IOL and the absence of angulation produces a broad surface of contact with the anterior capsules. In the presence of a small capsulorhexis, said contact could give rise to a stopper effect that might explain the higher prevalence of this complication with said design.

Kim et al. affirmed that patients who developed said syndrome in their series were younger (mean age = 55 years) than those who did not (mean age = 61 years). However, this difference was not significant from the statistical viewpoint. At any rate, the difference could have clinical significance, even more so taking into account that such an infrequent complication makes it very difficult to achieve statistical significance.

In another published series, affected patients had longer axial length, with the age of the 15 patients who developed said syndrome being between the fifth and sixth decade of life. As said series was a case and control study the age of affected and unaffected patients was similar because most likely this variable had been taken into account when selecting controls to make them similar to the cases. In the present series, the low frequency of two of the complications (CDS and ACP) render any comparison impossible. However, patients affected by CDS were a decade younger than those in the 3 remaining groups. The type of cataract exhibited by the patient was not specified in most reported cases. However, in the present series this complication was more frequent in patients exhibiting posterior subcapsular cataracts. As the latter is more frequent in young patients, it is difficult to determine whether the true risk factor is early age or the type of cataract.

The 3 cases discussed above were adequately treated with Nd–YAG capsulotomy, the most frequent procedure for managing the problem although at least 4 different approaches have been described. As in some cases Propionibacterium acnes was isolated in the sequestered fluid, some authors prefer to vacuum it out or drain it towards the anterior chamber carrying out a capsulotomy or simply breaking the valve mechanism, pushing the IOL back with a 30G needle in slit lamp.

**Anterior capsular phimosis**

Three patients developed ACP, a complication which has been related to diabetes mellitus, pseudoexfoliation, closed angle primary glaucoma, retinosis pigmentosa and myotonic dystrophy. As patients affected by retinosis pigmentosa or myotonic dystrophy are frequently treated at an early stage by means of cataract surgery; age could have become a confusion factor in these cases. Similarly, anterior uveitis was regarded for a long time as a risk factor for developing PCO until an article demonstrated that this apparent association was probably due to the fact that those patients were operated for cataracts at a younger age. The risk factors referred by the literature for this complication are scarcely represented in the present patients. This leads the authors to think that the approach proposed by some authors, i.e., preventive treatment for high risk patients applying YAG laser bursts in the early post-surgery period, is not applicable to the population of the present study. The mean age (73 years) was similar to that of the rest of the groups (excluding patients with CDS who exhibited a significantly lower mean age value). One of the patients who developed ACP had diabetes mellitus but none had glaucoma or pseudoexfoliation. It is worth noting that 2 were implanted with PhysIOL MicroSlim® IOL, a hydrophobic preloaded IOL with 0.7 mm diameter, similar to that of Akreos Adapt AO® but with thinner haptics. It could be that the characteristics that enable easy implantation through a very small incision render it vulnerable to centripetal forces which give rise to ACP and predispose said IOL to develop said complication. At any rate, all patients were successfully treated with relaxing incisions at the edge of the capsulorhexis.

In summary, the present study was not able to demonstrate a relationship of PCO with any of the studied variables. Complications derived from YAG capsulotomy are infrequent and therefore the patients need not to be examined systematically. The PCO incidence was similar in the 3 implanted IOLs. However, in the present cohort the patients who were implanted with Akreos Adapt AO® AO® experienced higher CDS incidence, while those who were implanted with a MicroSlim®
IOL exhibited higher ACP incidence. Younger age and presence of a posterior subcapsular component are probably risk factors for developing CDS.

Conflict of interests

J.J.G.L. received financial support (study grants) from Alcon, Novartis and MSD and has carried out unpaid consultancy for Bayer.

REFERENCES


