RESEARCH ARTICLE

Postoperative membranous proliferation outgrowth onto the anterior surface of hydrophobic acrylic intraocular lenses

Ying Lin[1],Hongbin Gao[2, 3],Yuhua Liu[1],Xialin Liu[1],Mingxing Wu[1],Lixia Luo[1], Bing Cheng[1], Yao Ni[1], Jiangna Chen[1], Jiaxuan Liu[1], Xinhua Huang[1], Yizhi Liu[1]

[1]*State Key Laboratory of Ophthalmology, Zhongshan Ophthalmic Center, Sun Yat-sen University, Guangzhou 510060, China*
[2]*Guangdong Province Hospital for Occupational Disease Prevention and Treatment; Guangdong Provincial Key Laboratory of Occupational Disease Prevention and Treatment, Guangzhou, Guangdong 510300, China*
[3]*Department of Toxicology, School of Public Health and Tropical Medicine, Southern Medical University, 1023 South Shatai Road, Guangzhou 510515, China*
The first four authors contributed equally to this publication.

Correspondence: Yizhi Liu and Xinhua Huang
E-mail: yzliu62@126.com
Received: July 06, 2015
Published online: July 28, 2015

Purpose: The aim of this study was to determine the correlation factors and features of membranous outgrowth onto the anterior surface of hydrophobic acrylic intraocular lenses. **Methods:** This study included 145 eyes from 135 consecutive patients who had cataract surgery with implantation of a single-piece, foldable, hydrophobic acrylic intraocular lens. Postoperatively, the IOL optic was examined by slit-lamp microscopy at 1 week and1 month to determine the incidence, extent, and correlation factors of membranous proliferation. If MP was present, we re-examined the patient monthly to monitor the condition.The extent of this proliferation was assessed using a clock-face representation of the IOL optic as the number of hours in which membranous proliferation could be identified. **Results:** Twenty-four eyes were excluded from analysis and 121 remaining eyes were studied. Membranous proliferation was documented in 46 (38.02%) of the pseudophakic eyes. Furthermore, the incidence of membranous outgrowth was greater in pseudophakic eyes characterized by older age, shorter axial length and more serious anterior segment vitreous opacity. Membranous proliferation was greater in the inferior (35.11%) and nasal quadrants (33.51%) than in the superior and temporal quadrants (where the incisions were made). The total area of membranous proliferation was slightly less than one quadrant (56.52%).**Conclusions:** Shorter axial length, older age, serious anterior segment vitreous opacity, and the inferior and nasal quadrants are risk factors for membranous proliferation on the IOL surface. Appreciation of these risk factors may lead to establishing procedures that willlessen anterior capsule opacification and capsule contraction syndrome simultaneously. **Financial disclosure(s):** The author(s) have no proprietary or commercial interest in any materials discussed in this article.

Keywords: Membranous outgrowth;Hydrophobic acrylic; Intraocular lenses; Cataract

To cite this article: Ying Lin, *et al*. Postoperative membranous proliferation outgrowth onto the anterior surface of hydrophobic acrylic intraocular lenses. MolMed Chem 2015; 2: e896. doi: 10.14800/mmc.896.

Introduction

Capsular opacification, or after-cataract, is the major complication of cataract surgery. It occurs due to migration, proliferation, and differentiation of residual lens epithelial cells (LECs). These LECs attempt to undergo normal differentiation or epithelial mesenchymal transition (EMT), forming heterogeneous groups of cells in the anterior capsule (anterior capsule opacification [ACO]) and posterior capsule (posterior capsule opacification [PCO]) [1].

The purpose of this study was to identify the risk factors

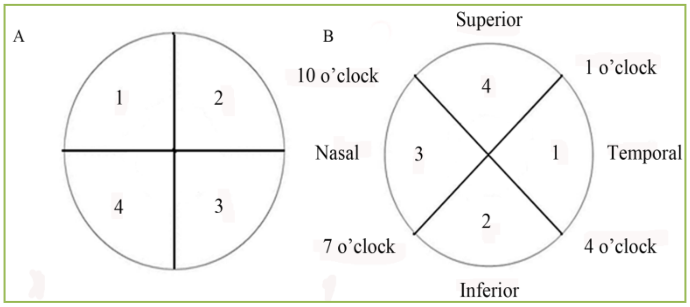

Figure 1. The extent of MP was assessed using a clock-face representation of the IOL optic as the number of area of clock hours in which membranous proliferation could be identified. Figure A shows the clock hour divisions commonly used in other studies. Instead, we divided the clock hours into 4 quadrants according to the position of the incision (Figure B). In all cases, the incision was made in the temporal region (Quadrant 1.). Quadrant 1: 1-4 o'clock. Quadrant 2: 4-7 o'clock. Quadrant 3: 7-10 o'clock. Quadrant 4: 10-1 o'clock.

for MP on the IOL surface. We found that some LECs can proliferate and migrate from the anterior capsular margin onto the intraocular lens (IOL) to form a membranous sheet with an accumulation of extracellular matrix. This membranous proliferation（MP）may be related to the ACO and capsule contraction syndrome [2].

We sought to elucidate the relationship between MP and ACO, and to determine which procedures can reduce ACO and capsule contraction syndrome simultaneously.

Patients and methods

This prospective study comprised 145 eyes from 135 consecutive patients who had cataract surgery at Zhongshan Ophthalmic Center from January 1 to August 1, 2014. Patients with ocular disease other than age-related cataract were excluded. Ocular axial length ranged from 22 mm to 26 mm. All studies of the patients were performed with the approval of the center's hospital ethics committee and conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from all patients. All surgery was performed by the same experienced surgeon (Yizhi Liu), using a standard quick-chop technique [3-5]. Phacoemulsification was performed with an Infiniti phacoemulsifier (Alcon Laboratories, Texas, USA). The surgical technique included a clear corneal incision in the temporal quadrant, a 5.5 mm continuous curvilinear capsulorhexis (CCC), phacoemulsification and aspiration, and in-the-bag IOL (SA60AT, Alcon, USA) implantation. Patients who had intraoperative complications, such as posterior capsule rupture, were excluded from the study. Eyes in which the margin of the anterior capsule did not completely cover the rim of the IOL optic because of excessive diameter or deviation of the CCC were also

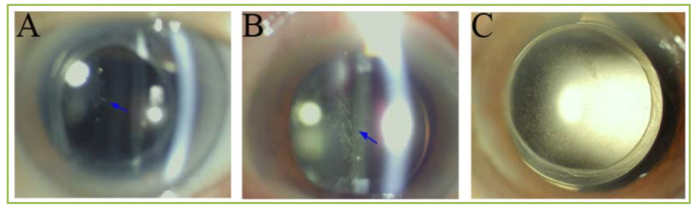

Figure 2. Anterior vitreous opacity. A: Grade 1, mild, slight vitreous opacities; B: Grade 2, moderate or severe, broad and dense vitreous opacities.C: A substance likely to be cells covered the entire anterior surface of the IOL at 1 week.

excluded.

Postoperatively, all patients received the same antibiotic eye drops for 1 month. One week and one month postoperatively, the pupil was dilated with tropicamide to allow examination of the IOL optic by slit-lamp microscopy, retroillumination, and diffuse illumination to document the morphology and extent of the cellular reaction following implantation. If MP was present, we re-examined the patient monthly to monitor the condition. The extent of proliferation was assessed using a clock-face representation of the IOL optic to identify the location of the MP. Whereas other studies have divided the 12 clock hours into four consecutive quadrants (Figure 1A) [6-7], we divided them into four quadrants according to the position of the incision (Figure 1B). Differences in quadrants were evaluated by variance analysis (ANOVA). A level of P <0.05 was considered statistically significant.

Basic descriptive statistics were calculated for all data gathered and are reported as mean ± SD or n (%), as appropriate. Univariate logistic regressions were applied to those parameters that might be associated with the development of an MP. The parameters tested included age, gender, right vs left eye, preoperative visual acuity, ultrasound total time, ultrasound total equivalent power, postoperative visual acuity, ocular axial length, diopter power of the IOL, and grade of anterior vitreous opacity. Risk factors with P-values <0.15 were further evaluated with multiple logistic regression analyses. All tests were two-tailed and a P-value of <0.05 was considered statistically significant.

According to the degree of vitreous opacities proposed by Koga *et al*[8], the degree of anterior vitreous opacity was classified as: Grade 1, mild, slight vitreous opacities (Figure 2A); or Grade 2, moderate or severe, broad and dense vitreous opacities (Figure 2B).

RESULTS

Correlation Factors

Table 1. Characteristics of patients enrolled in the study

Variable	Patients
Number of patients enrolled in study	145
Number of patients excluded from analysis	24
Number of patients examined (%)	121(83.45%)
Age (yrs)	72.24± 8.04 (range, 39-87)
Gender (female/male)	39/82
Eye (right/left)	66/55
Visual acuity	1.03± 0.66
Eyes that developed MP	46 (38.02%)
Ultrasound Time	0.59± 0.47
Ultrasound Power	13.49± 9.07
Axial length	23.61± 0.82
Diopter of IOL	20.05± 1.67
Postoperative Visual Acuity	0.16± 0.22
Number of clock hours with MP by quadrant	
Number of clock hrs with MP in quadrant 1 (temporal)	
Number of clock hrs with MP in quadrant 2 (inferior)	25
Number of clock hrs with MP in quadrant 3 (nasal)	
Number of clock hrs with MPin quadrant 4 (superior)	66
Number of quadrants affected in 46 eyes with MP	
One or less quadrant	63
Between one and two quadrants	
Between two and three quadrants	33
More than three quadrants	
Presence of vitreous opacity	
Anterior vitreous opacity Grade 1	26 (56.52%)
Anterior vitreous opacity Grade 2	11(23.91%)
	6 (13.04%)
	3 (6.52%)
	73(60.33%)
	48(39.67%)

Data are given as means± standard deviation whenever indicated.

Table 2. Summary of relationship variables and presence of MP in pseudophakic eyes

Variable	Univariate Analysis P Value	Multivariate Analysis* Odds Ratio	95% Confidence Interval	P Value
Age	0.0006	1.12	1.04-1.22	0.0018
Gender	0.2574			
Eye	0.2450			
Preoperative visual acuity	0.0322	0.62	0．28-1.37	0.2398
Ultrasound time	0.4755			
Ultrasound power	0.7419			
Axial length	0.0076	0.29	0．10-0.87	0.0276
Diopter of IOL	0.1189	0.86	0.50-1.49	0.5902
Postoperative visual acuity	0.2742			
Anterior vitreous opacity	<0.0001	11.11	4.17-33.33	<0.0001

*Only variables with a P value of less than 0.15 in the univariate analysis were included in the multivariate model.

Table 3. Differences among the 4 quadrants

Group*	1 Difference	1 P Value	2 Difference	2 P Value	3 Difference	3 P Value	4 Difference	4 P Value
1	—	—	-0.34	0.0014‡	-0.31	0.0030‡	-0.07	0.4806
2	0.34	0.0014‡	—	—	0.31	0.0030‡	0.26	0.0124‡
3	0.31	0.0030‡	-0.02	0.8141	—	—	0.24	0.0234‡
4	0.07	0.4806	-0.26	0.0124‡	-0.24	0.0234‡	—	—

‡ The mean difference is significant at the .05 level.
* 1=temporal quadrant; 2=inferior quadrant; 3=nasal quadrant; 4=superior quadrant.

No intraoperative complications occurred. A total of 24 eyes were excluded from the study because the rim of the IOL optic was not completely covered by the anterior capsule margin and the axial length was abnormal. The frequency and characteristics of MP on the IOL optic were evaluated in the remaining 121 eyes. Table 1 shows the patient

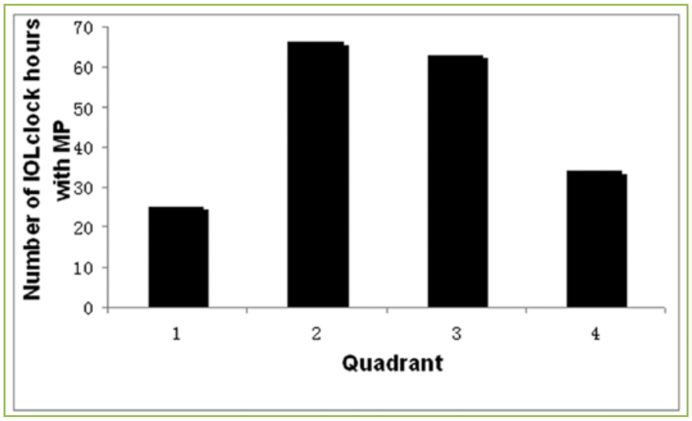

Figure 3. In 46 eyes with MP, the number of hours affected in each quadrant of the optic was determined. I.e., if an eye had MP in the area of 2-4 o'clock and in the area of 4-5o'clock, that optic was recorded as having 2 hours in quadrant 1 and 1 hour in quadrant 2. Clock hours affected were 25, 66, 63, and 33 in quadrants 1-4, respectively. Quadrants: 1= temporal; 2=inferior; 3= nasal; 4=superior.

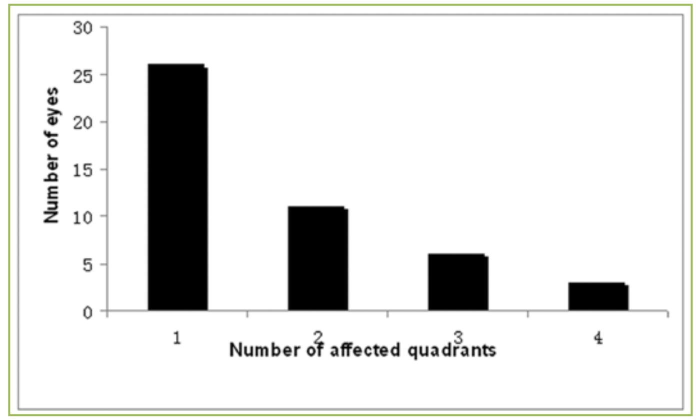

Figure 4. Number of IOL optic quadrants affected in each of 46 eyes that exhibited MP. 1 = 3 clock hours or less. 2= 3-6 hours. 3 = 6-9 hours. 4 = 9-12 hours. Most eyes (26) had MP in one quadrant only, while 11 eyes were affected in two quadrants, 6 in three quadrants, and only 3 in all four quadrants.

characteristics and outcome features. There was no statistical difference in MP between 1 week and 1 month (P>0.05). MP was detected in 46 eyes (38.02%) at 1 week. The membrane occurred as a transparent monolayer originating from the edge of the capsulorhexis. In all eyes except one, LEC growth was limited to the margin of the capsulorhexis and did not regress to the center. In one eye, the monolayer covered the entire anterior surface of the IOL at 1 week（Figure 2C), but disappeared at 1 month. In all cases, the anterior capsule was in contact with the IOL optic. This supports findings in previous studies describing the importance of the relationship of cell proliferation onto the optic[9].

We did not find any correlation between MP and gender, right vs left eye，ultrasound total time, ultrasound total equivalent power, or postoperative visual acuity. However, univariate analysis did identify an inverse relationship between MP and age, preoperative visual acuity, axial length, diopter power of the IOL, and grade of anterior vitreous opacity. Multivariate logistic regression analysis was used to re-examine those characteristics identified in the univariate analyses for which P<0.15. This stepwise selection confirmed the relevance of age, axial length, and anterior segment vitreous opacity. The incidence of membranous outgrowth was greater in pseudophakic eyes characterized by shorter axial length, older age, and more serious anterior segment vitreous opacity (Table 2).

Features

Using the new method of dividing the lens surface according to the location of the incision, we found that the inferior (35.11%) and nasal (33.51%) quadrants were more likely to exhibit MP than the superior (18.09%) and temporal quadrants (13.30%) at 1 week. (See Table 3 and Figure 3.) Total area of MP did not substantially exceed that encompassed by a single quadrant (56.52% [Table 1 and Figure 4]).

We combined retroillumination and diffuse illumination with slit-lamp microscopy (Figure 5A, B, C) to analyze the morphology of MP, because the strong reflex from the IOL surface sometimes did not allow visualization of certain areas. Using the three methods, we could combine the three pictures and better visualize the total optic. The photographs in Figure 5 A, B, C are from the 1-month examination of a patient who had MP coveringal most three quadrants. Slit-lamp examination and microscopy showed that the MP was continuous with the capsular opening and concentric to the center of the optic, and it appeared to consist of elongated cells extending from the anterior capsular margin. The dendritic fan-shaped MP displayed an apical portion directed toward the central optics (Figure 5A).

DISCUSSION

AcrySof SA60AT

All of the patients received the recently introduced foldable hydrophobic acrylic IOL (AcrySof SA60AT, Alcon,USA), which is now commonly used. This IOL is a single-piece, square-edged acrylic with a 6.0 mm optic diameter and no haptic angulation. The SA60AT material is a co-polymer of 2-phenylethyl acrylate and 2-phenylethyl methacrylate with a water content of 0.3% [10].

It has been reported that with a poly (methyl methacrylate [PMMA]) IOL, MP occurs in 40% to 80% of patients [11-12].

In our study, 46 patients (38.02%) displayed MP, which extended from the anterior capsule margin onto the IOL optic soon after cataract surgery.

Kurosaka and Kato[13] found that the incidence and extent of MP were significantly greater on acrylic IOLs than on PMMA and silicone IOLs, due to improved biocompatibility of the acrylic IOL. Interestingly, Shah *et al* found that the incidence of ACO is lowest with acrylic lenses and highest with plate haptic silicone IOLs [1].

We speculate that several factors may account for the conflicting findings mentioned above. First, cells forming ACO may derive from the germinal zone, whereas cells forming MP derive from the rim of the capsulorhexis. Second, all of these cells come from the rim of the capsulorhexis and the total number of cells is relatively constant. Cells that have more potential for adhesion and remain in the capsule will cause ACO, and those having more potential for migration and outgrowth onto the IOL surface will result in MP (Figure 5F). Third, MP cannot be ruled out as an index of lens epithelial cell proliferative activity [14]. Among those proteins related to the extracellular matrix, fibronectin promotes maximal migration of LECs, whereas type IV collagen promotes maximal adhesion of LECs in vitro; fibronectin is present in the aqueous humor of patients with cataracts [15].

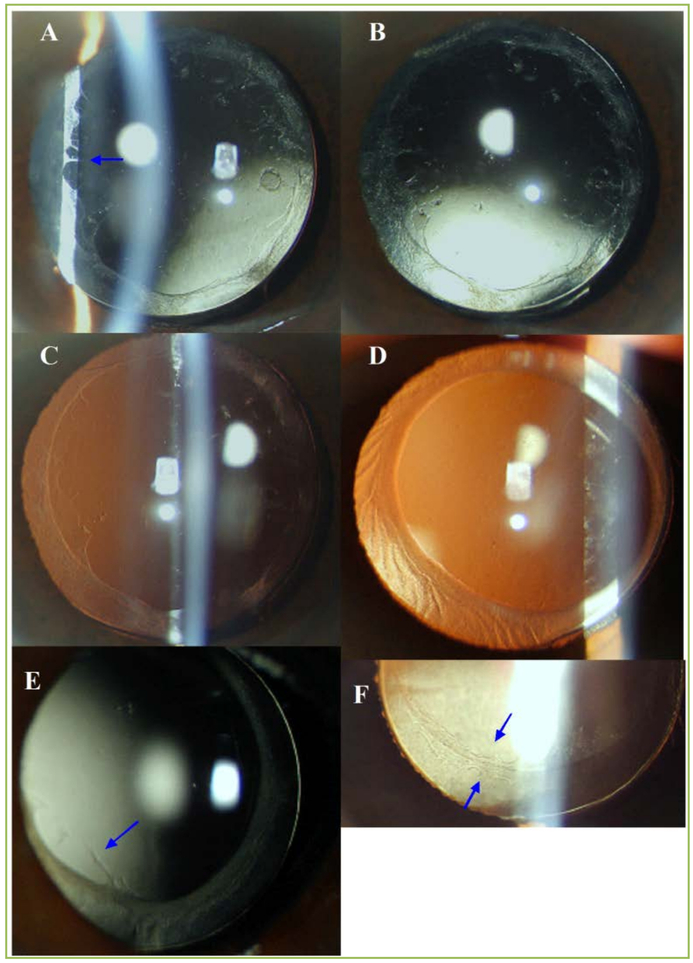

Figure 5. The photographs in Figure 5 A, B, C are from the 1-month examination of a patient who had MP covering almost three quadrants. We combined retroillumination and diffuse illumination with slit-lamp microscopy (A, B, C) to analyze the morphology of MP.A: Slit-lamp microscopy shows MP continuous with capsular opening; arrow points to the center of the optic. B: Diffuse illumination shows MP. C: Retroillumination shows MP. D: Linear margin at 1 month. MP retracted and became a thinner membrane close to the capsulorhexis. E: Discontinuity in the process of regression. The retraction was usually contiguous (as in Figure D), but one patient exhibited a gap between the MP and the margin of the capsulorhexis at 1 month (E). F: Membranous proliferation between anterior capsule and the IOL and on the surface of the IOL.

Correlation Factors

In contrast to our results, Lenis and Philipson did not observe any correlation between MP and other factors, such as age, capsulorhexis size, or presence of pseudoexfoliation [11].Reported risk factors for contraction of the anterior capsule opening include diabetes mellitus [16], uveitis [17], old age, and instability of the blood-aqueous barrier [18]. Risk factors for PCO include young age [19] and pseudoexfoliation[20]. Pathologically, contraction of the anterior capsule opening and PCO are considered to result from similar mechanisms; however, the risk factors for the two disorders are not identical. In particular, they have opposite relationships to age. If the cells derived from capsule contraction syndrome were those with greater potential for migration, whereas cells from PCO were those with greater potential for adhesion, the two cell types would not have opposite relationships with age. This can account for the different relation between age and contraction of the anterior capsule opening and age and PCO.

Older patients may have different levels of growth factors in the anterior chamber compared to younger patients, and this may be related to the potential of LECs for adhesion and migration. We had collected some samples of aqueous humor to elucidate which factors influence cell activity and the ratio of migration factors to adhesion factors, which could simultaneously lessen ACO and capsule contraction syndrome.

In patients who had shorter ocular axes, shallower anterior chamber depth, narrower space in the anterior ocular segment, and higher vitreous pressure, the operation was difficult to perform. The postoperative inflammatory reaction was severe and may account for the shorter ocular axial length and serious MP observed.

Some studies have found that ACO [21] and MP [7] were related to anterior chamber laser flare; proliferation at the anterior interface occurs on the portion of the implant surface exposed to the aqueous humor. We propose that both the anterior and the posterior environments influence lens epithelial cell proliferation on the anterior implant surface. In our study, we found that vitreous opacity was correlated with proliferation; inflammatory factors from the vitreous humor may have contributed to the process of membrane formation, because some cells and proteins could move freely between the anterior and posterior chambers with the aqueous humor.

Furthermore, we propose that human lens epithelial cell proliferation and migration in vivo are initiated by loss of contact inhibition as a result of surgical trauma. We also propose that humoral factors are released into the aqueous humor as a result of postoperative breakdown of the blood-aqueous barrier [11] .

Our results with regard to ultrasound total time and ultrasound total equivalent power were similar to those of Kruger *et al* [9]. Ultrasound time and power influence intraoperative LEC damage. In addition, the prolonged operating time resulting from relatively large quantities of fluids used to irrigate the anterior chamber might influence intraoperative LEC damage, while more time and power may also promote LEC.

We speculate that the location of the incision was correlated with MP, which has not been previously reported. Obviously, the location of the incision affects the operative procedure. Both the CCC and the aspiration of the cortex is limited in a small space that is difficult to reach, which may influence the removal of the LECs and the potential proliferative ability of LECs. Further study is needed to elucidate these effects. Moreover, the influence of gravity may increase the density of certain factors in some quadrants. If the concentration of some factors related to LEC migration in the inferior quadrant was denser than in the other quadrants, the MP may be more serious in this quadrant.

Morphology

Lens epithelium generates an endogenous physiological electric field (EF) [22], in which LECs proliferate, migrate, re-orient, elongate and differentiate into lens fibers. LECs migrate in one of two directions in vivo. Either they migrate toward the equator and elongate and trans-differentiate to become lens fiber cells, or they migrate in the opposite direction, toward the front of the lens, to compensate for ongoing apoptosis of LECs as the epithelium turns over. This EF may be related to the dendritic nature of fan-shaped membranous growth, which exhibits an apical portion directed toward the central optics (Figure 5A).

Usually, over continued follow-up, MP disappeared within a few months or retracted as a thinner membrane close to the capsulorhexis (Figure 5D). However, there were some exceptions, as described below. One patient exhibited a gap between the MP and the margin of the capsulorhexis at 1 month (Figure 5E), but this gap had completely disappeared at 2 months.

Another patient displayed a substance likely to be composed of cells extending throughout the entire IOL surface at 1 week (Figure 2 C)**,** but this proliferation disappeared at 1 month. This may have occurred because LECs were not immediately removed by aspiration when they emerged on the surface. The LECs were dispersed throughout the viscoelastic material and remained there until the viscoelastic substance was removed at the end of surgery. It is possible that the LECs adhered to the capsule or IOL surface, proliferated, and migrated. These two cases suggest that certain factors of the aqueous may affect the metabolism of residual LECs on the surface of the IOL.

A third patient displayed differences between the left and right eyes, with serious MP occurring in one eye (Figure 5A, B, C) and none in the other. Individual variations in the intraocular conditions that render the surrounding conditions sufficient for LEC proliferation cannot be ruled out. This could explain the differences in proliferative capacity between individual patients or different eyes.

Possible Etiologic Mechanisms

In general, it is believed that LECs from the equator of the capsular bag play a minor role in the development of anterior cell migration and capsule opacification [23]. LECs that proliferate onto the anterior IOL surface are thought to originate from the anterior capsule close to the capsulorhexis. We tend to share this opinion, based on our clinical observation of 121 cases and on various observations reported in the literature. A number of etiologic mechanisms may contribute to MP, as discussed below.

Residual LECs proliferate and transform metaplastically into myofibroblasts after cataract removal. Proliferating LECs migrate from the anterior capsule margin onto the anterior optic surface, accompanied by an accumulation of extracellular matrix. It is possible that an increased inflammatory response to surgery in some patients promotes formation of this fibrous membrane.

Fibrous metaplasia of LECs usually occurs between the IOL optic and the inner surface of the anterior capsule [24].

The fibrous membrane is present near the anterior capsule, and its contraction decreases the anterior capsule opening. These findings suggest that lens epithelial cell outgrowth from the capsule margin onto the IOL may be related to capsule contraction syndrome[25] .

Multiple extracellular molecules may be involved in the in vivo adhesion and migration of lens epithelial cells. This suggests that multiple independent mechanisms can be involved in this response or that multiple interdependent steps are involved in either the adhesion or migration of these cells in response to extracellular matrix proteins.

It has been postulated that fibronectin of serum origin resulting from postoperative damage to the blood-aqueous barrier could play an important role in lens epithelial cell proliferation and migration [26]. Notably, fibronectin is not found in significant quantities in adult human lens capsule [27], but fibronectin immunoreactivity has been demonstrated in the acellular proteinaceous membrane on explanted IOLs.

In dose-response experiments, fibronectin promoted maximal migration at lower concentrations in comparison with type IV collagen and laminin[28].

Ultimately, a sound understanding of the molecular mechanisms directing lens epithelial cell adhesion and migration should provide direction for the development of novel biopharmaceutical agents to prevent vision-disturbing complications after cataract surgery. Further studies are necessary to prove that the membrane reported in this study is the LEC sheet and to determine which factors in the aqueous humor are related to MP.

Acknowledgments

The authors are grateful to all the patients, families, and normal control volunteers for their participation in this investigation. This study was supported by the National Natural Science Foundation of China (Grant No. 81320108008), the Natural Science Foundation of Guangdong Province, China (Grant No. S2012020010878) and Youth Project of Fundamental Research Funds of State Key Laboratory of Ophthalmology (Grant No.2011Q09 and 2014QN04), and Medical Scientific Research Foundation of Guangdong Province (Grant No. B2012126).

References

1. Shah SK, Praveen MR, Kaul A, Vasavada AR, Shah GD, Nihalani BR. Impact of anterior capsule polishing on anterior capsule opacification after cataract surgery: a randomized clinical trial. Eye (Lond) 2009; 23:1702-1706.
2. Kurosaka D, Ando I, Kato K, Oshima T, Kurosaka H, Yoshino M, et al. Fibrous membrane formation at the capsular margin in capsule contraction syndrome. J Cataract Refract Surg 1999; 25:930-935.
3. Liu X, Cheng B, Zheng D, Liu Y. Role of anterior capsule polishing in residual lens epithelial cell proliferation. J Cataract Refract Surg 2010; 36:208-214.
4. Liu Y, Zeng M, Liu X, Luo L, Yuan Z, Xia Y, et al. Torsional mode versus conventional ultrasound mode phacoemulsification: randomized comparative clinical study. J Cataract Refract Surg 2007; 33:287-292.
5. Wang Y, Xia Y, Zeng M, Liu X, Luo L, Chen B, et al. Torsional ultrasound efficiency under different vacuum levels in different degrees of nuclear cataract. J Cataract Refract Surg 2009; 35:1941-1945.
6. Pande MV, Spalton DJ, Kerr-Muir MG, Marshall J. Cellular reaction on the anterior surface of poly(methyl methacrylate) intraocular lenses. J Cataract Refract Surg 1996; 22 Suppl 1:811-817.
7. Pande MV, Spalton DJ, Marshall J. In vivo human lens epithelial cell proliferation on the anterior surface of PMMA intraocular lenses. Br J Ophthalmol 1996; 80:469-474.
8. Koga T, Ando E, Hirata A, Fukushima M, Kimura A, Ando Y, et al. Vitreous opacities and outcome of vitreous surgery in patients with familial amyloidotic polyneuropathy. Am J Ophthalmol 2003; 135:188-193.
9. Kruger AJ, Amon M, Schauersberger J, Abela-Formanek C, Schild G, Kolodjaschna J. Anterior capsule opacification and lens epithelial outgrowth on the intraocular lens surface after curettage. J Cataract Refract Surg 2001; 27:1987-1991.
10. Park TK, Chung SK, Baek NH. Changes in the area of the anterior capsule opening after intraocular lens implantation. J Cataract Refract Surg 2002; 2:1613-1617.
11. Koch MU, Kalicharan D, van der Want JJ. Lens epithelial cell layer formation related to hydrogel foldable intraocular lenses. J Cataract Refract Surg 1999; 25:1637-1640.
12. Lenis K, Philipson B. Lens epithelial growth on the anterior surface of hydrogel IOLs. An in vivo study. ActaOphthalmolScand 1998; 76:184-187.
13. Kurosaka D, Kato K. Membranous proliferation of lens epithelial cells on acrylic, silicone, and poly(methyl methacrylate) lenses. J Cataract Refract Surg 2001; 27:1591-1595.
14. Ibaraki N, Ohara K, Miyamoto T. Membranous outgrowth suggesting lens epithelial cell proliferation in pseudophakic eyes. Am J Ophthalmol 1995; 119:706-711.
15. Vesaluoma M, Mertaniemi P, Mannonen S, Lehto I, Uusitalo R, Sarna S, et al. Cellular and plasma fibronectin in the aqueous humour of primary open-angle glaucoma, exfoliative glaucoma and cataract patients. Eye (Lond) 1998; 12:886-890.
16. Kato S, Oshika T, Numaga J, Hayashi Y, Oshiro M, Yuguchi T, et al. Anterior capsular contraction after cataract surgery in eyes of diabetic patients. Br J Ophthalmol 2001; 85:21-23.
17. Davison JA. Capsule contraction syndrome. J Cataract Refract Surg 1993; 19:582-589.
18. Kato S, Suzuki T, Hayashi Y, Numaga J, Hattori T, Yuguchi T, et

al. Risk factors for contraction of the anterior capsule opening after cataract surgery. J Cataract Refract Surg 2002; 28:109-112.

19. Jamal SA, Solomon LD. Risk factors for posterior capsular pearling after uncomplicated extracapsular cataract extraction and plano-convex posterior chamber lens implantation. J Cataract Refract Surg 1993; 19:333-338.

20. Kuchle M, Amberg A, Martus P, Nguyen NX, Naumann GO.Pseudoexfoliation syndrome and secondary cataract. Br J Ophthalmol 1997; 81:862-866.

21. Miyake K, Ota I, Miyake S, Maekubo K. Correlation between intraocular lens hydrophilicity and anterior capsule opacification and aqueous flare. J Cataract Refract Surg 1996; 22 Suppl 1:764-9.