doi: 10.17116/engoftalma20151313-3

Analyzing causes for opacification of acrylic IOLs

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Aim – to study the nature of intraocular lens (IOL) opacification depending on the patient's ocular status and general condition. **Materials and methods.** A total of 9 patients (9 eyes) with 3—6 year history of progressive IOL opacification were enrolled. All the IOLs were acrylic (either hydrophilic – 7 cases, or hydrophobic – 2 cases). Two patients had their IOLs exchanged due to opacification. Six patients earlier underwent glaucoma surgery. Two patients were type 2 diabetic. Slit lamp biomicroscopy and optical microscopy were used for IOL examination. **Results.** The surface of hydrophilic acrylic lenses appeared bumpy because of multiple variously shaped translucent granules separated by a chaotic network of furrows and microfractures and located predominantly in the optic zone. In a more severe case, a bowl-shaped impression was observed in the area of opacification. Surface changes of hydrophobic acrylic lenses were in the form of isolated and confluent glistening formations (microcavities). **Conclusion.** Signs of IOL degradation develop over a long period of time (3—6 years, in our experience) and mostly involve the anterior surface of the lens optic. Ocular comorbidity, glaucoma in particular, as well as other surgery and/or therapeutic treatment following IOL implantation may contribute to its opacification. Analysis of published data and own observations suggest that hydrophobic IOLs should be preferred in patients with concomitant diseases, especially diabetes mellitus. Granular deposits, if accumulate, may lead to deformation of the lens optic, as confirmed by the bowl-like impression in one of the explanted hydrophilic IOLs.

Keywords: *opacification, IOL, acrylic, hydrophilic, hydrophobic.*

Vestnik oftal'mologii 2015; 3: 64-70

It is widely known that the longevity of an implant is determined by material's properties, specifically, by its structure and strength. Despite the significant progress in the area of new materials and intraocular implants production technologies, we often encounter cases of intraocular lens (IOL) opacification and color alteration [1]. Maintaining the stability of implants as well as their biocompatibility with eye tissues is, therefore, one of the manufacturers' priorities. Yet the question as to what the reasons of IOL destruction in the postoperative period are, has no definite answer. There is data indicating that structural changes in IOLs may be due to incompleteness of implant polymerization process as well as negative effects of bioactive media or polymer destruction products on the IOL material. It has also been noted that biological stability of an implant may depend on free radicals that are generated and accumulated during the multistage polymer processing, including thermal (pressing and compression molding) and mechanical treatment (turning, polishing, and grinding), thus, initiating implant depolarization [2]. Signs of IOL destruction in the form of opacification or, perhaps, changes in its optical characteristics, usually develop within the timeframes from 3—5 months to 3-plus years [3—5]. The risk has been reported for IOLs made of polymethyl methacrylate (PMMA), silicone, and hydrogel [6—10]. Currently popular acrylic IOLs with varying degrees of hydrophilicity or hydrophorbicity (hydrophilic IOLs with 18—38% water content and hydrophobic IOLs with that up to 1.5%), despite all their benefits, also possess the above mentioned disadvantages. As shown by analysis of acrylic hydrophilic IOL reimplantation cases, lens opacification is the most common indication for the second intervention (60% of cases), while severe optic aberrations and lens power miscalculations account for the rest 40%. As for hydrophobic IOLs, the necessity of reimplantation usually arises from lens dislocation (31%) or, again, power miscalculation (34%) [11].

As a rule, it is the surface of the lens that gets damaged, but intralenticular opacities may also occur [1,12]. Due to the variety of locations of pathological changes within the IOL, it has been proposed to distinguish 3 types of opacifications. Type 1 implies the central area of both anterior and posterior IOL surfaces being opacified, type 2 stands for anterior involvement only, while type 3 opacification is meant to be total, i.e. occupying the entire lens optic [5]. Studies of explanted hydrophilic IOLs revealed a collection of polymorphic granules in the area of alteration that could not be mechanically removed [13].

The possibility of concomitant pathology and subsequent surgery having an effect on the state of the lens has been studied by both Russian and foreign researchers. Their results show that type 2 diabetes mellitus patients are at particularly high risk of hydrophilic acrylic IOL degradation with the frequency of lens opacification as high as 21.5% (while that in people with non-complicated anamnesis is only 14.3%) [14]. Examination of the aqueous humor from the anterior chamber and blood serum in these patients revealed an increased content of

calcium and phosphates, which are, in author's opinion, the substrate for crystalline deposits found on the surface of acrylic hydrophilic lenses [15]. The risk group for alterations within the hydrophilic acryl should also include patients with such concomitant diseases or conditions as glaucoma, hypertension, renal failure, gout, arthritis, hypothyroidism, and hypercholesterolemia [1,5,12,14,16,17]. Some data indicates that the risk is also higher in case of blood-ocular barrier failure [13]. There have been cases of severe opacification of hydrophilic acrylic IOLs after vitreoretinal surgery involving the use of silicone oil, which appeared to be capable of irreversible adhesion to the contacting lens surface [6]. There is also an opinion that superficial deposits on hydrophilic lenses can be explained by its exposure to silicone from silicone-containing packages [4]. An interesting case of reversible bilateral opacification of hydrophilic acrylic IOLs has been reported. A 56-year-old female suffering from diabetic retinopathy and chronic myeloid leukemia underwent bilateral phacoemulsification and implantation of MI Akreos-60 hydrophilic lenses. In a month she presented with complaints of decreased vision in both eyes. The examination revealed bilateral IOL opacification and macula edema. The latter was treated with intravitreal bevacizumab (Avastin). Two months after the injections the transparency of both IOLs was almost completely restored. The authors, however, admit that the role of anti-VEGF therapy in resolving the opacities is unclear and requires further investigation [18].

In view of the aforesaid, hydrophobic acrylic IOLs have been suggested as an alternative treatment option. Hydrophobic acrylic IOL opacities differ from those typical of hydrophilic lenses and appear as single or multiple vacuole-like glistening microcavities. There are, however, a relatively small number of cases of PMMA, silicone, and hydrophilic acrylic IOLs showing a glistening effect as well [8]. The said changes may manifest within the first year after the implantation and variously intensify later with the occurrence rate as high as 86.5% of operated patients [3]. New techniques of lens manufacturing, particularly those involving injection molding with solidification, allow a decrease in the number of cases of hydrophobic IOL opacification. Quantitative comparatives have been drawn between opacified hydrophobic acrylic lenses manufactured in 2003 and 2012. Thus, the average density of pathological elements within the lens optic appeared as high as 315.7 and 39.9 microcavities/mm^2 respectively [19]. It is thought that hollow inclusions in hydrophobic acryl result from temperature fluctuations: the microcavities formed during material polymerization become filled with water as the temperature of the surrounding medium decreases, at that they are only visible due to the difference in refractive indices. As shown in an experiment, dehydration of a heated hydrophobic IOL leads to contraction and partial (or even complete) disappearance of the "bubbles" [20]. It is presumed that the formation of microcavities during material polymerization is determined by accumulation of hydrophilic (oligomerous) impurities. Then, as the osmotic pressure gradient between the IOL and surrounding liquid medium increases, hydrophilic inclusions transform into vacuole-like microcavities. This process continues until the thermal equilibrium is achieved. Cases of hydrophobic acrylic IOL replacement are rather rare, since their opacifications usually have no significant impact on visual acuity. There is also opposition against the assumed possibility that decreased contrast sensitivity and increased aberrations associated with considerable visual discomfort are due to the above-described IOL changes [8]. Other authors have drawn their attention to acrylic hydrophobic IOLs, such as AcrySof lenses by Alcon. In particular, they point to the high probability of lens opacification after a triple procedure (i.e. phacoemulsification, IOL implantation, and vitrectomy). They have also reported brown rings on the surface of explanted hydrophobic lenses that are, in authors' opinion, of protein origin. Calcifications (typical of hydrophilic lenses) have not been found [21].

IOL manufacturing technologies constantly improve and lens storage and packing requirements increase. Promotional booklets and lens descriptions often contain such statements as "Glistening-free IOL" implying that this particular lens is just unable to opacify. However, as daily practice shows, measures taken to overcome a problem do not always lead to its complete solution. Moreover, as IOL changes are obviously multifactorial in causation, further studies in this field are required.

The present work is **aimed** at studying features and analyzing causes of acrylic IOL opacifications.

Material and methods

The study involved 9 patients (9 eyes) aged from 32 to 72 years previously treated in different clinics and referred to a laser surgeon at the Research Institute of Eye Diseases with the following provisional diagnoses: secondary cataract, exudative pupillary membrane, and precipitations on the anterior surface of the IOL. According to patients' histories, 7 of them had received phacoemulsification with IOL implantation for non-complicated age-related cataract and 1 — for cataract complicated with chronic recurrent uveitis and diabetes mellitus. There was also a single case of secondary IOL implantation into an aphakic eye, which had been operated on in early childhood due to a congenital cataract. It has been established that IOL opacifications developed 3 to 6 years after surgery. It is also known that all the IOLs were acrylic (7 hydrophilic and 2 hydrophobic) produced in either Europe, or USA. In cases of centrally located opacifications a significant decrease in vision acuity was noted (down to 0.04—0.3). In two cases the vision was moderately deteriorated (down to 0.5—0.6), which is likely to be due to more posterior and more peripheral location of opacifications (it was the posterior capsule and not the body of the lens that got opacified in these patients,

moreover, the changes were outside the optic zone and, therefore, could only be found under mydriasis). It should be noted that none of the hydrophobic IOL cases presented any visual complaints. A subsequent reimplantation was performed in two patients. The remaining 7 patients could only be examined and photographed at their first visit and were not available for the follow up. The anamnesis of 6 patients also indicated pre-existing non-compensated glaucoma, for which they were surgically treated within the timeframe from 1 week to 2 years after the cataract surgery. In the meanwhile they were prescribed maximal hypotensive regimens that included beta-blockers, carbonic anhydrase inhibitors, and latanoprost. Two patients had type 2 diabetes mellitus. Biomicroscopic appearance of the opacified IOLs was studied and captured with a BQ 900 Haag Streit slit lamp (Switzerland) and EOS 350D digital camera (Canon, Japan). For optical coherence tomography of the anterior segment a Visante OCT by Carl Zeiss Meditec (Germany) was used. In two cases the explanted hydrophilic acrylic lens was examined under an Opton digital microscope (Germany).

Results and discussion

All hydrophilic IOL opacifications were superficial. In 4 cases they were located right behind the pupil and roughly agreed with its shape and area (Fig. 1). It should be specified that central changes were typical of patients with operated glaucoma. In 1 case the opacification was diffuse and involved the entire lens including the haptics. In 2 patients the optic centers of hydrophilic IOLs remained clear, while their peripheries were occupied by either circular or semicircular opacities composed of separate "petals" (Fig. 2 and 3). Biomicroscopy of hydrophilic IOL opacities allowed to determine their typical pattern: multiple variously shaped translucent granules separated by a chaotic network of furrows and microfractures, the surface of the damaged IOL looking uneven. An attempt to clean the lenses using low-energy non-destructive laser radiation did not yield the desired result.

In hydrophobic acrylic IOLs, opacities were located at different levels but closer to the anterior surface of the lens and looked like isolated or grouped microcavities of varying size dispersed mostly within the optic area. They also presented the typical glistening appearance under certain lighting conditions.

The two explanted IOLs were studied particularly. Patient S., 72 years of age, had ultrasound phacoemulsification with IOL implantation at the Moscow Ophthal-

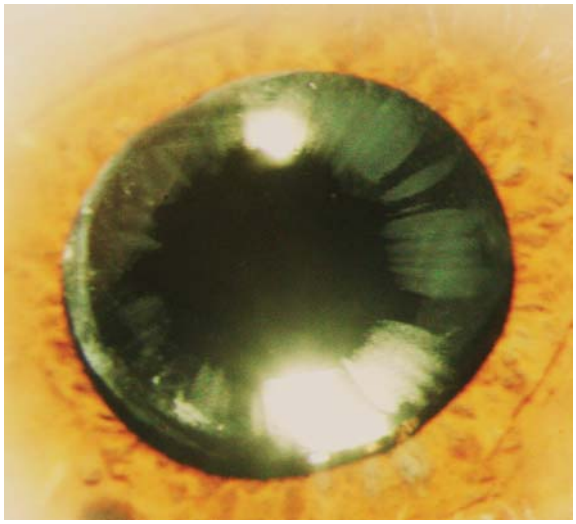

Fig. 2. **Biomicroscopic appearance of a circular ring opacity composed of separate "petals" and located on the anterior surface of a hydrophilic IOL outside its optic zone.**

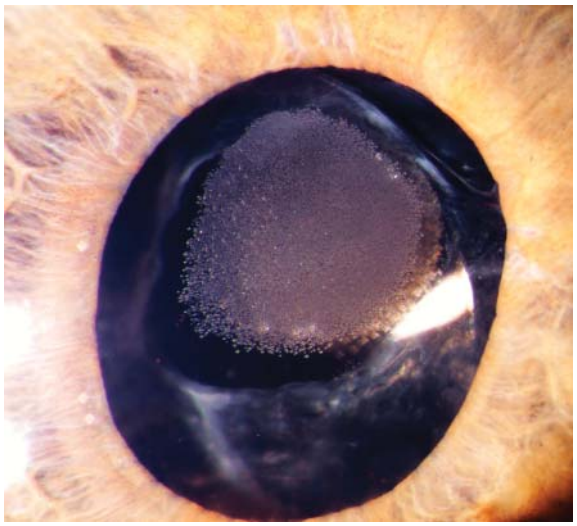

Fig. 1. **Biomicroscopic appearance of opacities on the anterior surface of a hydrophilic IOL within its optic zone.**

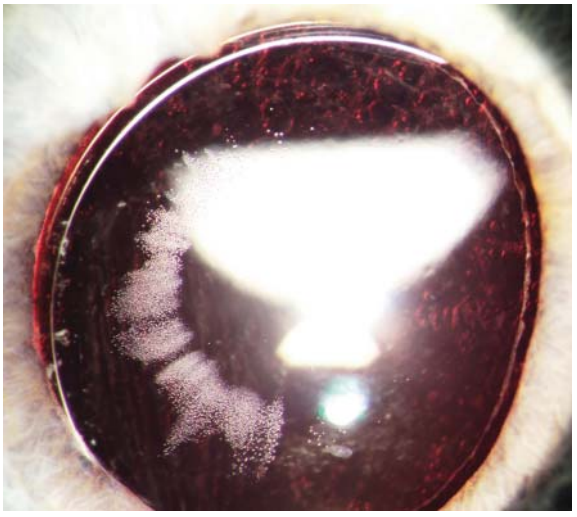

Fig. 3. **Biomicroscopic appearance of a semicircular opacity located closely to the anterior surface of a hydrophilic IOL.**

mological Clinical Hospital for an immature cataract in her right eye. The implanted lens was a LS-312-1Y hydrophobic surface coated hydrophilic acrylic lens by Oculentis (Germany). Three years after the surgery the patient was referred to the Research Institute of Eye Diseases due to complaints of deteriorated vision in the right eye. She was diagnosed with IOL opacification and offered a reimplantation. As for her left eye, it had been also operated on a year before that, however, the IOL (we were unable to establish its type) maintained clarity. The patient was known to have type 2 diabetes mellitus and central chorioretinal dystrophy. Light optical microscopy revealed a total diffuse opacity of the IOL surface involving both optic and haptics (Fig. 4). The changes had the appearance of a solid white coating consisting of microgranules, which, when merging, formed an irregular uneven relief on the surface of the lens. These deposits did not cause lens deformity, so it maintained proper configuration.

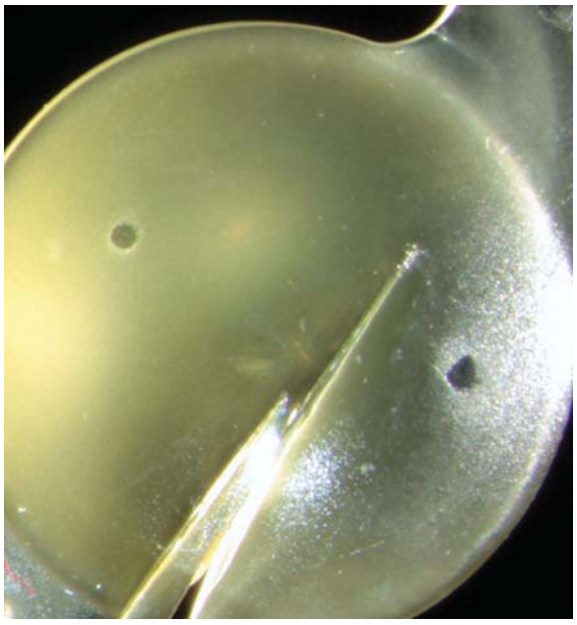

Fig. 4. **Light microscopic image of the hydrophobic surface coated hydrophilic acrylic IOL explanted from patient S. Total opacification of the entire lens surface.**

Patient G., 71 years of age, diagnosed with bilateral immature cataract underwent ultrasound phacoemulsification on both eyes with a one-month interval at the Research Institute of Eye Diseases and was implanted with two hydrophilic acrylic IOLs of the same model, specifically Micro+A 123 by PhysIOL (Belgium). In 6 years the patient presented with complaints of decreased vision in her right eye. The examination revealed a right-sided opacification of the lens optic (Fig. 4), while the other IOL remained clear. Ocular comorbidity included open-angle glaucoma stage 2a-b in both eyes. Because of uncontrolled elevation of intraocular pressure following cataract extraction in the right eye, unilateral glaucoma surgery was performed 2 weeks after the first intervention. During this period the patient maintained the maximal multidrug hypotensive regimen. As for the left eye, glaucoma surgery was unnecessary. According to OCT of the anterior segment of the right eye, the biconvex poste-

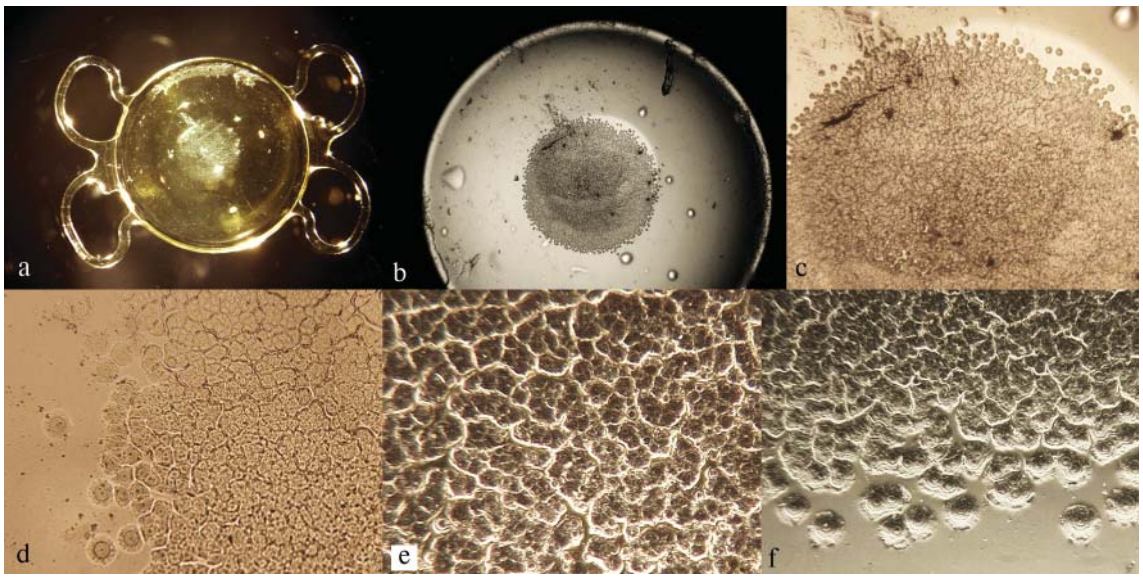

Fig. 5. **Light microscopic image of the hydrophilic acrylic IOL explanted from patient G.**

a — general appearance of the lens with an opacity in its center; b — microscopic appearance of the opacity; c—d — the defect consists of multiple polymorphic granules; e — the central area of the lens defect is occupied by irregular polygons separated by differently directed furrows; f — at the periphery of the defect the lens surface is uneven due to isolated round or polygonal figures with concentric protuberances and dome-like elevations

rior chamber IOL was well-centered within the capsular bag. Its anterior surface was optically non-transparent due to a circular opacity in the optic zone behind the pupil with a diameter of about 2.5 mm (Fig. 5 a, b). Unlike the intact periphery of the lens, the damaged area was rough. As shown by optical microscopy, the defect consisted of multiple polymorphic granules of varying size that were rather dense and exhibited a trend to merge (Fig. 5 c, d). More precisely, the central area of the defect was occupied by irregular polygons separated by differently directed furrows, and, thus, resembled cracked earth (Fig. 5e), while its periphery was full of isolated round or polygonal figures (however, those located more proximally tended to merge) with concentric protuberances and dome-like elevations (Fig. 5f). Generally speaking, surface microrelief of the defect was irregular and bumpy. Moreover, a shallow bowl-like impression was noted in the area of the opacity. An attempt of mechanical cleaning of the IOL was unsuccessful. The posterior surface of the lens optic, including the center, maintained clarity. The haptics were also intact.

Conclusion

Both hydrophilic and hydrophobic acrylic IOLs are liable to opacification. Signs of IOL degradation develop over a long period of time (3—6 years, in our experience) and in case of a hydrophilic lens mostly involve the center of its anterior surface. Ocular comorbidity, glaucoma in particular, as well as other surgery and/or therapeutic treatment following IOL implantation may contribute to its opacification. Analysis of published data and own observations suggest that hydrophobic IOLs should be preferred in patients with concomitant diseases, especially diabetes mellitus. The presence of destructive changes in the center of the lenses may indirectly indicate their photodamage. The question remains as to what are the reasons for peripheral (peri-equatorial) lens opacification. After having studied two explanted hydrophilic IOLs, we suppose that superficial granular deposits, if progress, are able to cause deformation of the lens optic, as confirmed by the bowl-like impression in one of the lenses. The results received are preliminary and determine the necessity for future studies, particularly, chemical analysis of the deposits detected on the lens surface.

Author contributions:
Study conception and design — A.G.
Acquisition and handling of data — A.G., A.F., I.N., A.K.
Statistical analysis of data — V.S., A.G.
Drafting of manuscript — A.G.
Critical revision — A.F.

The authors declare no conflict of interest.

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