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Posterior chamber silicone intraocular lens for the correction of myopia: an experimental study in rabbits

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ABSTRACT: Purpose. *To establish whether ocular lesions arise after implantation of posterior chamber silicone intraocular lenses (IOL) for the correction of high myopia.*
Methods. *Twenty-three posterior chamber silicone IOL were implanted in 23 eyes of the same number of pigmented rabbits. After different follow-up time (from one week to one year) the eyes were enucleated and processed for histopathological study after determining the protein concentration in the acqueous humor. The IOL were removed for staining and examination, and adhered cells were counted. Ten eyes analogous to those operated upon were used as controls.*
Results. *Intense inflammation was observed in the early postoperative period in all cases. Protein concentration in the acqueous humor was initially high and decreased over time, though without reaching normal values at one year. Mono- and multinucleated cells were seen adhering to the IOL, though they decreased in number over time and were practically absent after one year. Friction between the posterior surface of the iris and the IOL had no clinical repercussions. The only pigment accumulations were in the iris and in the peritrabecular zone. There were no siginificant differences in the accumulation of granules in relation to IOL diameter or power. Excluding three cataracts morphologically similar to traumatic cataracts, five lens opacifications were observed: two were anterior subcapsular cataracts, and the other three were only precapsular deposits. The IOL had no synechiae to the ocular tissues.*
Conclusions. *Opacification of the lens is the main concern with implantated posterior chamber silicone IOL. Larger series of eyes must be analysed to establish the true incidence and reversibility of these opacities. (Eur J Ophthalmol 1999; 9: 276-83)*

KEY WORDS: Myopia, Intraocular lenses, Histopathology

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INTRODUCTION

Research continues in the surgical correction of high myopia, with the aim of developing new methods that combine minimal eye injury and immediate, predictable and stable refractive results. The difficulties of securing this combination of advantages are the main cause of current controversy in refractive surgery.

Corneal procedures are less invasive than intraocular approaches, though cicatrization problems and the irreversibility of the former limit their predictability and efficacy (1).

Intraocular lenses (IOL) offer precise and stable correction from the first day onwards, as they do not depend on cicatrization (2, 3).

However, implantation requires invasive surgery. Before the posterior chamber lens was developed, two IOL solutions were available for the correction of my-

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opia, Baykoff's angle support lens (4) and the iris fixation (claw or Worst-Fechner) lens (5). Both may cause endothelial cell changes. The novelty of the posterior chamber lens is its implantation within the posterior chamber, which reduces the risk of damaging the endothelium.

Although Fyodorov's original idea of implanting a high myopia IOL in the posterior chamber of phakic eyes involved a model with the optic located in the area of the pupil and anterior chamber, and haptics fixed in the posterior chamber, a number of design modifications have subsequently been introduced (6, 7). At least three different models based on Fyodorov's lens are currently employed in clinical trials, with a new design entirely located in the posterior chamber over the anterior capsule of the lens (8-11). These IOL are soft and foldable, which reduces friction-induced damage to the ocular tissues. The implantation is totally reversible, for the IOL is not fixed to either the iris or angle, and is easily implanted, no materials different from those habitually used in cataract surgery are required.

However, this is the first case in which implantation is performed in the posterior chamber with the lens *in situ*, and little is known of the mechanisms underlying lens damage caused by IOL, since all morphological studies to date have been carried out in aphakic eyes after cataract surgery. Thus, despite the promising features of this new IOL, its location raises a series of uncertainties regarding the possibility of chronic inflammation, cataracts or pigmentary dispersion syndrome.

The present experimental study in rabbits, investigated whether the implantation of posterior chamber silicone IOL caused ocular lesions.

METHODS

Posterior chamber silicone myopia IOL

The posterior chamber IOL used in the present study were manufactured by Chiron-Adatomed and consisted of a single piece of silicone (polydimethyl siloxane). The biconcave optic is 5.5 mm in diameter, with a thickness that varies according to the refractive power. As the IOL is biconcave, it is thickest at the periphery, varying from 0.8 mm for –8D to –17D IOL, to 1.1 mm for –18D to –21.5D implants. The radius of the posterior surface is constant (9.9 mm). The haptics are 0.15 mm thick, and are located on both sides of the optic zone. The length of the haptics dictates the diameter or total length of the IOL. For each power the following diameter IOL are manufactured: 11/11.5/12/12.5/13. The dioptric power ranges from –8 to –21.5 diopters, in 0.5D steps (Fig. 1).

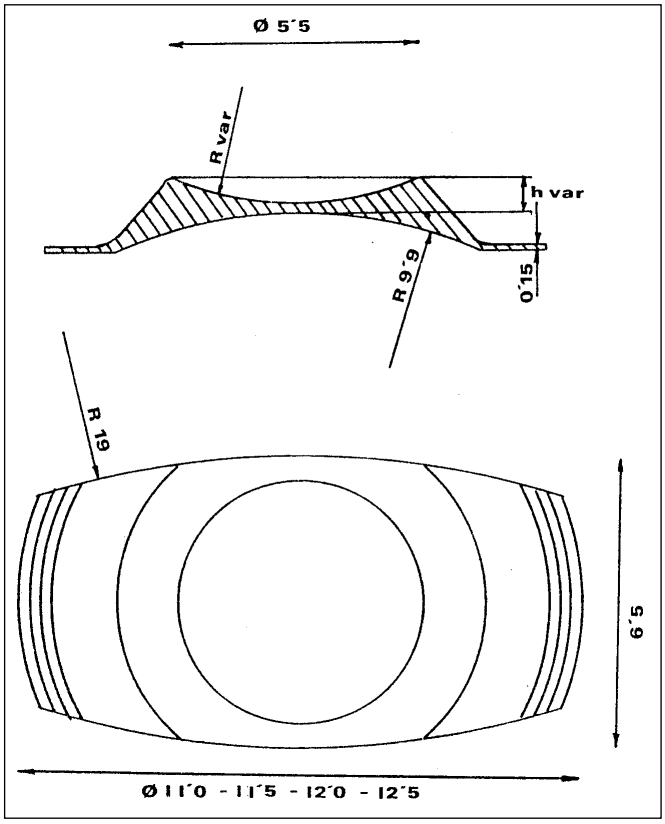


Fig 1 - *Schematic drawing of the posterior chamber silicone myopia IOL.*

Experimental model

The study was conducted in Spanish giant pigmented rabbits. Twenty-three IOL implantations were performed, distributed into five groups with different follow-up times (1 week, 1 month, 3 months, 9 months and 1 year). The IOL were distributed so that one of each type was used in every group for total diameter (short: diameter <12 mm; long: diamter ≥12 mm) and thickness (thin: power <18D; power ≥18D). Losses in the course of the experiment required the introduction of additional animals. The definitive groups were thus as

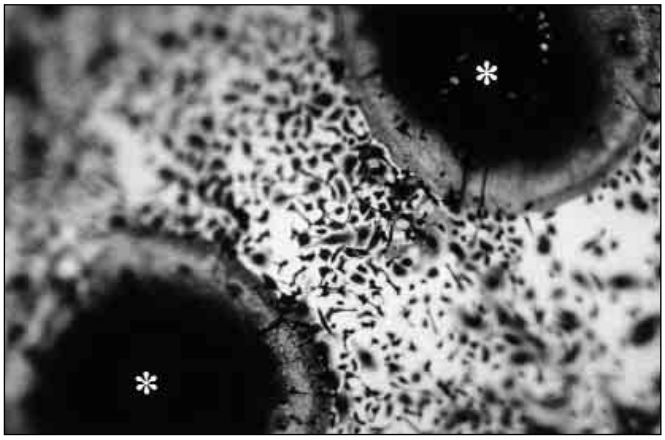


Fig 2 - *Two giant multinucleated cells (asterisks) and multiple mononucleated cells in an IOL stained with modified Diff-Quiz (DQ x 200).*

follows: 1 week, 4 IOL; 1 month, 4 IOL; 3 months, 5 IOL; 9 months, 5 IOL; 1 year, 5 IOL. Ten eyes analogous to those subjected to implantation were used as controls.

Dimensions of the rabbit eye

The cornea is prominent, large, and more curved than in humans. The mean horizontal and vertical diameters are 15 and 13.5-14 mm. Curvature radius ranges from 7 to 7.5 mm, with a thickness of 0.3-0.4 mm on average. The lens is larger and more spherical than in humans, though its composition and functional characteristics are similar. The anteroposterior diameter is about 7 mm, while the equatorial dimension range from 9 to 11 mm. The radius of the anterior and posterior surface is 5.3 and 5 mm, respectively (12).

Surgical procedure

Surgery was performed under the surgical microscope in the Research Center of La Fe University Hospital (Valencia, Spain). All animals were sedated with ketamine hydrochloride (50 mg/ml) prior to manipulation. The pupil was dilated with a drop of tropicamide. A 15-degree blade was used to make a 6.5-mm corneal incision. Viscoelastic was injected above the iris and between the iris and the anterior capsule of the lens. The IOL was then implanted in the posterior chamber with the long axis vertical, sliding the lower haptics under the iris and the upper posteriorly. The anterior chamber was irrigated with saline solution to extract the viscoelastic and 1% acetyl choline, after which the incision was closed with 8-00 silk suture. Antibiotics (tobramycin), 2% policarpine and dexamenthasone ointment were applied during the first week after surgery.

Postoperative follow-up

The rabbits were housed individually under standard conditions, with free access to food and water. European Union regulations for the handling of laboratory animals were complied with at all times. The rabbits were checked daily for the first 15 days after surgery, and monthly thereafter, with special emphasis on signs of inflammation and complications.

Enucleation

Eyes were enucleated at different times after surgery for the different groups (1 week, 1 month, 3 months, 9 months or 1 year).

Specimen fixation and processing

Both eyes were enucleated and examined under the biomicroscope then immersed in 2% formaldehyde at 4°C for at least one week. Posteriorily, the eyes were dissected according to the Assia and Apple scleral window technique (13), with minor modifications to give a better view of the IOL position and the rest of the structures of interest in each case. Photographs were taken then the eyes were embedded in paraffin for processing, and multiple thin (5-8 µm) anteroposterior sections were stained with hematoxylin-eosin and examined under the light microscope.

Histopathological study

The IOL were stained with modified Diff-Quiz, May Grand Wald Giemsa, and examined under the light microscope, then adhered cells were counted. A distinction was made between mono- and multinucleated cells, and cell location on the haptics and optic was recorded (Fig. 2). All multinucleated cells adhering to the IOL surface were recorded, and the number of mononuclear cells was evaluated by calculating the mean of five fields under 100x magnification.

In each selected field we counted the cells within the frame of the microscope eyepiece for correct centering and focusing of the photographs.

Study of aqueous humor

After enucleation, samples of acqueous humor were collected from 16 implanted eyes and 4 controls, using a 30G needle on a sterile insulin syringe. These samples were stored in Ependorff and frozen at –80°C until study, when the samples were thawed to room temperature and processed for quantitative assay of total proteins using the brilliant indocyanine direct method.

Statistical analysis

The chi-square test was used to compare qualitative variables, and analysis of variance (ANOVA) for the pre- and postoperative measurements of all groups at different follow-up times. Linear regression analysis was done when there were two quantitative variables. Statistical significance was taken as $p<0.05$.

RESULTS

Inflammation

Intense inflammation lasting 5 to 14 days in the immediate postoperative period was observed in all cases. The inflammatory process started with the formation of a cyclitic membrane immediately after surgery, and occasionally in the course of surgery itself. Intense corneal edema developed secondary to inflammation, preventing visualization of the anterior pole structures. Among the histological alterations related to the inflammatory process in the eyes enucleated in the first week after surgery, there were zones of the iris and/or ciliary processes with epithelial loss, inflammatory infiltration, and marked vascular congestion. These alterations were only observed in this early group of rabbits, and were no longer present in eyes enucleated three weeks after surgery.

The total protein concentrations in aqueous humor were highest in the first week after surgery (Tab. I). After one month they were still high, but lower than at one week. The protein content decreased further after three months, though statistical significance was only reached after nine months and at one year. Thus, although the late follow-up concentrations approached normal values, significant differences persisted with respect to the controls.

The IOL retrieved during the first week after surgery had the largest numbers of mono- and multinucleated cells on the haptics (Tab. II), the differences in the number of cells being significant between this group and those at the other follow-up times. However, no multinucleated cells adhered to the optic, which had a few mononucleated cells. The IOL removed after one month had fewer multinucleated cells on the haptics, and the optic was practically free of cells. The optic was only invaded by multinuclated cells in the eyes enucleated three months after surgery. Both cell types decreased in subsequent groups, to practically zero fo the IOL removed at nine months.

On assess possible relations between IOL size and inflammation as reflected by protein concentration and the number of cells adhering to the IOL, no significant differences were seen between either inflammatory parameters or IOL size as reflected by power and diameter. Likewise, no significant relations were recorded between acqueous humor protein levels and the duration of early postoperative inflammation.

Lesions of the iris and/or ciliary process

In no case did we observe iris transillumination defects or pigment deposits in the epithelium. The controls had significantly more pigment granules in the iris and trabecular zone. No significant differences were recorded in the accumulation of granules in relation to IOL diameter or power. No significant differences were recorded between the different follow-up groups as regards pigment accumulation in the iris or the number of peritrabecular granules.

Lens injury

Nine lens opacifications were recorded (Fig. 3). Three had morphological evidence of capsular rup-

ture and cell proliferation, characteristic of traumatic cataracts. Another three had slight opacification around a posterior synechia; in two of them, deposits were observed only on the lens capsule, and were linear. The third had opacification resembling a subcapsular cataract of the remaining three cases, two were anterior subcapsular cataracts,and the other merely had pigment deposits but no true cataract. In the eyes enucleated in the first week postsurgery, lens opacification could not be evaluated because the fibrin membrane and corneal edema prevented observation of the lens. Opacification was significantly related to the duration of the inflammatory period, but not to either protein concentration or the number of cells adhering to the IOL. Significant relationships were observed between opacification and all types of deposit, though no correlation was established between opacification and IOL size. The existence of cellular and non-cellular deposits appeared to be related to the intensity of surgical trauma.

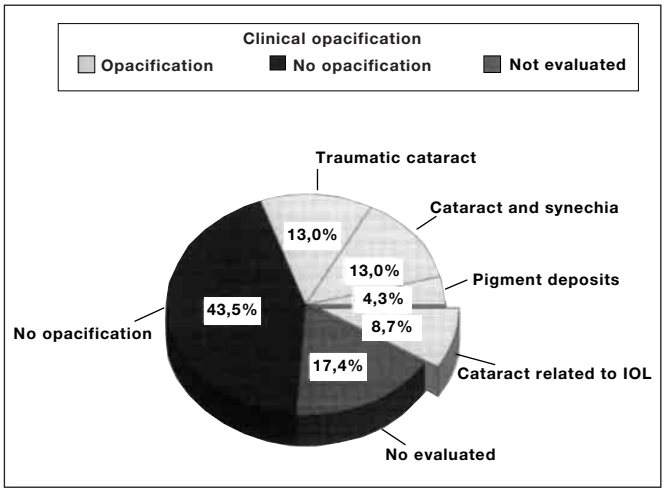


Fig 3 - *Percentage of lens opacifications.*

After three months of follow-up, four IOL (17.4%) suffered luxation of one or both haptics to the anterior chamber. When this was detected, the eye was enucleated, as the IOL had never been luxated more than one month. There were fewer non-cellular deposits in the case of anterior or anterior/posterior chamber (i.e., totally or partially luxated) IOL than in posterior chamber IOL. Peritrabecular granules were more numerous in the eyes with partially luxated IOL.

TABLE I - PROTEIN CONCENTRATION IN AQUEOUS HUMOR (mg/dl)

	Follow-up time					
	1 wk	1 mo	3 mos	9 mos	1 yr	Control group
Mean	139.00	129.64	124.15	95.70	86.25	56.60
SD*	1.68	2.20	6.72	17.83	21.00	19.97

SD* standard deviation

TABLE II - NUMBER OF CELLS ADHERING TO THE IOL (Mean ± standard deviation)

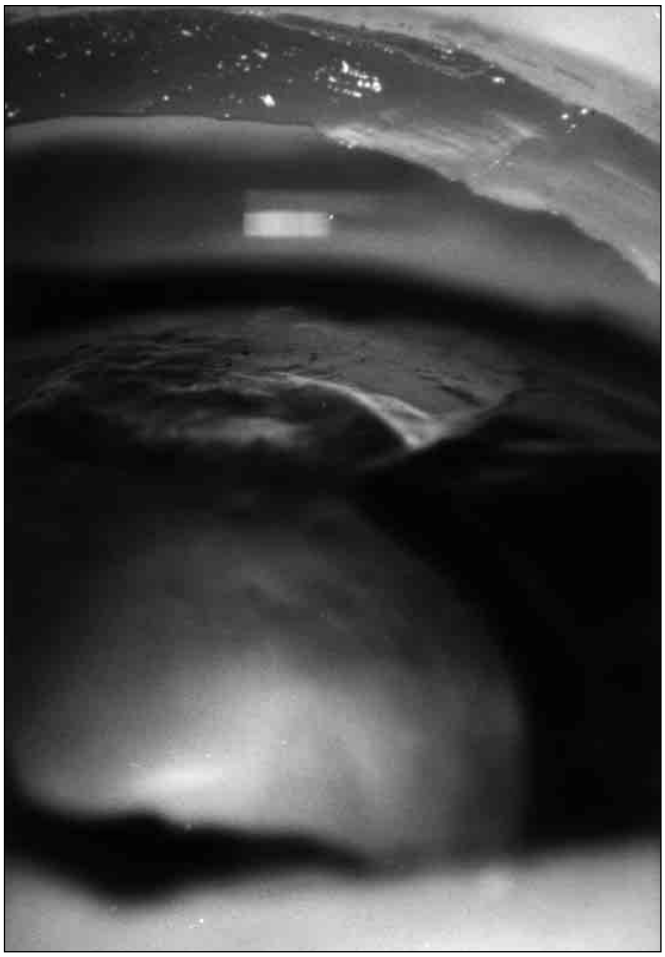
	Follow-up time				
Type of cells	1 wk	1 mo	3 mos	9 mos	1 yr
H-MU	75.0 ± 7.1	29.5 ± 9.2	27.5 ± 19.4	0.7 ± 0.6	0
O-MU	2.0 ± 2.8	0.5 ± 0.7	8.7 ± 6.4	2.3 ± 3.2	0
H-MO	45.0 ± 7.1	8.5 ± 2.1	16.3 ± 17.9	1.6 ± 0.6	2.7 ± 1.3
O-MO	14.0 ± 1.4	12.0 ± 8.5	23.3 ± 21.8	1.7 ± 1.1	1.5 ± 0.6

H-MU indicates multinucleated cells on haptics, O-MU, multinucleated cells on optic; H-MO, mononucleated cells on haptics; O-MO, mononucleated cells on optic

DISCUSSION

Posterior chamber silicone myopia IOL are specifically designed to be used in phakic high myopia patients. They are positioned between the posterio surface of the iris and the anterior surface of the lens. The posterior surface of the IOL is concave, vaulting over the anterior lens capsule to leave space for the acqueous. The haptics of the IOL rest on the anterior zonular fibers.

An IOL was implanted in an eye from a human cadaver, after donation of the cornea. Photographs were taken under the surgical microscope of the different relations between the lens and ocular structures (Fig. 5-above). When both models (human and rabbit) are compared (Fig. 5-above and below), it can be seen that the IOL in the rabbit eye is in a forced position because of the sphericity of the lens. However, the relationships between the IOL and the ocular structures are the same in both.



▲

Fig 4 - *Deposits over the crystalline capsule.*

▲ ***Above***

▲ ***Below***

Fig 5 - *Images showing the relationship between the IOL, lens and iris.* ***Above:*** *In an eye from a human cadaver.* ***Below:*** *In an eye from a rabbit.* ▶

IOL implantation in rabbits is difficult because of frequent positive pressure – leading to collapse of the anterior chamber when opened – and the formation of a fibrin membrane that produces synechiae between the iris and IOL, making surgery difficult. Studies in humans make little mention of these aspects, emphasis being placed on the advantages of the simple and rapid implantation (8-11).

Postoperative inflammation with a plastic reaction and intense fibrin formation is habitual in rabbits, and was observed in all cases in the present study (14, 15).

These inflammatory manifestations decreased with time, with no posterior episodes to suggest that the IOL was responsible. Protein concentration in the acqueous humor also gradually decreased, though the levels had not returned to normal one year after surgery. In contrast, after one year the IOL was free of adhered cells. Consequences of the early postoperative inflammation were synechiae between the iris and capsule,and possibly also the deposits on the IOL surface.

Regarding pigmentary dispersion attributable to friction between the IOL and posterior iris, no clinical manifestations were observed, though the histological study showed slight subclinical manifestations reflected in the significantly greater pigment accumulations in the iris and peritrabecular zone in the operated rabbits than controls. The literature on this particular IOL reports no clinically manifest pigmentary dispersion (8-11).

The present study confirms the possibility of cataract formation following the implantation of posterior chamber silicone IOL. However, cataracts were not seen in all cases, so other etiological factors must also be involved. Except for the three cataracts that we suspected were of traumatic origin, all could be accounted for as stages in the formation of an anterior subcapsular cataract. In three cases opacification was slight and developed around a posterior synechia because of the inflammatory stimuli. In the other two cases, no etiological agent other than the IOL was established. Apart from the three suspected traumatic cataracts and those around posterior synechiae, a relationship was identified between opacification and IOL size, as the two cases with opacifications morphologically corresponding to anterior subcapsular cataracts were eyes implanted with thick IOL (>18D). A significant correlation was established between opacity and the duration of inflammation, though not with protein concentration in the acqueous humor or the number of cells adhering to the explanted IOL.

A possible explanation for the above findings might be as follows. During the inflammatory process cells and detritus deposit in different structures of the anterior pole. These deposits gradually clear over time, but a space or chamber forms between the posterior chamber silicone IOL and the lens, where acqueous flow is diminished. This largely (though not entirely) prevents normal clearance of the detritus and cells released by the inflammation. This could in certain cases produce precapsular deposits. If this situation were to continue, the precapsular deposits would impede correct epithelial function, limiting exchanges between the acqueous humor and the epithelium, hence favoring cell damage. When epithelial cell lesions arise, the epithelium begins to proliferate, forming a capsule similar to the anterior capsule; the cells enveloped by this pseudocapsule degenerate into a magma, forming the anterior subcapsular cataract. In other words, the posterior chamber silicone IOL does not in itself induce cataract formation, but the limitations it imposes on acqueous flow predispose to cataract formation under conditions such as uveitis, angle block and trauma.

If this physiopathological mechanism is correct, then extraction of the IOL in the first months after the appearance of opacification (i.e., when only deposits are involved) could well permit clearing of the lens, since the epithelial cells have not yet been damaged.

Fechner reported an anterior central subcapsular opacity in 8 out of 45 patients who had a transparent lens prior to implantation of an IOL, after between one and two years of follow-up. Of the 13 patients who had incipient opacification before surgery, only one showed an increase in opacification at follow-up (10). However, Asseto recorded no cataracts in a series of 15 implants (8). Similar observations apply to the study by Ertürk, though that series comprised only 8 cases (11). Menezo and Cisneros, in a larger series, observed opacities in 10% of cases (personal communication).

It is worth noting the absence of adhesions to the ocular tissues, for even in those cases where posterior synechiae were observed, these extended from the iris to the anterior capsule of the lens, facilitating extraction of the IOL when necessary. Furthermore, the procedure was fully reversible.

The present results suggest that opacity of the lens is the main concern as it was observed in 26.3% of the eyes. This opacity may be reversible provided the IOL is explanted within the first three months after its appearance.

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