Surface Cytologic Features on Intraocular Lenses

Can Increased Biocompatibility Have Disadvantages?

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Objective: To compare the anterior surface cytologic features and effect on blood-aqueous barrier of polymethyl methacrylate, silicone, and hydrogel intraocular lens (IOL) implants to give an indication of their biocompatibility.

Methods: This prospective study was performed at an English-teaching hospital. Ninety eyes were randomized to receive a polymethyl methacrylate, silicone, or hydrogel implant. A standardized surgical protocol was performed by a single surgeon using phacoemulsification. Patients were seen at intervals for 1 year. Measurements of visual acuity, contrast sensitivity, and anterior chamber laser flare and cells were obtained; and an assessment of lens cytologic features using specular microscopy of the anterior IOL surface was performed.

Results: Visual acuity and contrast sensitivity were not significantly different among the 3 groups. Hydrogel IOLs were associated with fewer inflammatory cells on their surface than polymethyl methacrylate and silicone IOLs (P < .001), but with significantly more lens epithelial cells (LECs) (P < .001). Patients with hydrogel implants without LECs had greater blood-aqueous barrier breakdown than those with LECs.

Conclusions: The hydrogel IOLs were associated with a reduced inflammatory cell reaction but had many more LECs on their anterior surface. Those IOLs associated with increased blood-aqueous barrier damage did not develop LECs. If an IOL is too biocompatible, then it may incite the growth of LECs over its surface, which could have disadvantages.


Small-incision surgery for phacoemulsification has encouraged the development of a range of foldable intraocular lenses (IOLs) and, although these have undergone considerable in vitro assessment, their in vivo behavior remains to be fully evaluated. There are 3 major aspects to biocompatibility within the human eye: the effect on the blood-aqueous barrier (BAB),1,2 the cellular reaction on the anterior surface of the lens,3,5 and the effect on the posterior capsule. Blood-aqueous barrier changes can be assessed by the measurement of anterior chamber flare and cell levels using the laser flare and cell meter.6 With modern lenses and good surgery, postoperative BAB changes are largely influenced by the surgical technique.7-9 Cells on the anterior surface of the implant can be examined in vivo postoperatively using specular microscopy and have been used extensively as a method of assessing the foreign body response to the IOL.5,10-12 The effect on the posterior capsule consists of lens epithelial cell (LEC) proliferation and metaplasia leading to posterior capsular opacification (PCO).13,14 Postoperatively, the cytologic features on the anterior surface of the lens implant are composed of 3 distinct cell populations15 that have been studied extensively with polymethyl methacrylate (PMMA) IOLs, and each of these has a different time course.16,17 Small, round, and fibroblast-like cells appear on the implant surface soon after surgery and peak at 1 month.16 These are macrophages probably cleaning up the surface of the IOL.3,16 Epithelioid and giant cells appear a few weeks after surgery on PMMA IOLs; they peak in numbers at 3 months19 and then progressively decline and probably represent a chronic foreign body response to the IOL. The third cell population consists of LECs that migrate from the anterior capsulorhexis edge where it comes into contact with the optic surface.18-21 On PMMA IOLs, the migration of LECs is scanty, peaking at around 1 month after surgery, and then the cells gradually and completely regress, leaving a fibrotic capsulorhexis rim devoid of cells by 3 months postoperatively.

This study compares the anterior surface cytologic features on 3 different IOLs: a rigid PMMA IOL and 2 foldable lens implants, one made of silicone and the other of a hydrogel polymer. We describe unique cytologic changes on the hydrogel IOLs.

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**RESULTS**

Ninety eyes of 90 patients were enrolled, with 30 patients randomized to each IOL group. There was no difference in age and sex distribution among the 3 groups. The average age was 73.6 years (age range, 60-90 years).

**VISUAL ACUITY AND CONTRAST SENSITIVITY**

LogMAR visual acuity at 1 year was assessed for the patients who had not developed notable retinal problems reducing their acuity below 0.30 (20/40 OU). Of the 30 patients with PMMA IOLs, 3 had age-related macular degeneration and 1 had a central retinal artery occlusion. The mean acuity, excluding these patients, was 0.05. Of the 28 patients seen at 1 year with hydrogel IOLs, 1 had age-related macular degeneration; excluding this patient, the average acuity was 0.04. In the group with silicone IOLs, none had any retinal pathological features and the mean acuity was 0.02. All of the lens groups had visual acuities equivalent to 20/20 OU at 1 year if age-related macular degeneration and central retinal artery occlusion are excluded and there was no statistically significant difference among the 3 groups ($P = .86$).

Best-case Pelli-Robson contrast sensitivities at 1 year were 1.45 for PMMA, 1.41 for hydrogel, and 1.49 for silicone ($P = .31$). There was a trend for patients with silicone IOLs to have better contrast sensitivities than those with hydrogel IOLs ($P = .13$; 95% confidence interval, 0.02-0.14).
LEC CHANGES

Figure 1 demonstrates the percentage of patients with LECs on the optic surface of the 3 lens types at each point during follow-up. At 1 month, 20 of 30 patients with hydrogel IOLs had LECs compared with 12 of 30 with PMMA IOLs and 0 of 30 with silicone IOLs ($P<.001$). Patients with hydrogel IOLs are significantly more likely to have LECs on their anterior IOL surface for longer than patients with PMMA and silicone IOLs ($P<.001$). Figure 2 shows the number of quadrants in which LECs were found on the IOL surface. With PMMA and silicone IOLs, only a few LECs are seen adjacent to the capsulorhexis margin (Figure 3). They reach a peak between 1 week and 1 month after surgery and thereafter regress, so that by 6 months after surgery few patients with these IOL types have any LECs on the optic surface, leaving a fibrotic capsulorhexis rim. Hydrogel IOLs have greater numbers of these cells that do not regress. In 15 (50%) patients with hydrogel IOLs, the LECs formed a confluent sheet along the capsulorhexis rim for $360^\circ$ between 1 and 6 months after surgery (Figure 4), often mirroring the capsulorhexis margin (Figure 5). By 6 months after surgery, they appear to be stable and further spread ceases (Figure 6, A, B, and C). In some areas, what appear to be nuclei can be seen within the cells (Figure 6, B and C). The LECs did not cover the visual axis on any of the IOLs (Figure 4). On hydrogel IOLs, only minor changes were seen after 3 months, with the cells persisting in all patients.
INFLAMMATORY CELLULAR CHANGES

Figure 7 shows the percentage of patients with small cells on the IOL surface for the 3 IOL types. At 1 month after surgery, small cells were present on 4 of 30 hydrogel IOLs, 11 of 30 PMMA IOLs, and 15 of 30 silicone IOLs ($P = .01$). Patients with hydrogel IOLs had a shorter duration ($P < .001$) and lower grades ($P < .001$) of small cells than patients with silicone or PMMA IOLs (Figure 7 and Figure 8).

Figure 9 shows the percentage of patients with epithelioid cells on the lens surface of the 3 IOL types. At 1 month after surgery, epithelioid cells were present on the anterior surface of 0 of 30 patients with hydrogel IOLs compared with 11 of 30 with PMMA IOLs and 1 of 30 with silicone IOLs ($P < .001$). During follow-up, epithelioid cells were present for significantly longer on PMMA IOLs than hydrogel and silicone IOLs ($P < .001$).

Figure 10 shows the grade of epithelioid cells present at each interval and shows that PMMA IOLs were associated with significantly higher grades than hydrogel or silicone IOLs ($P < .001$).
We were interested in determining why a few patients with hydrogel IOLs did not develop LECs on the anterior surface of the lens implant after surgery. Patients who developed LECs were compared with those without LECs. There was no significant difference in the preoperative flare and cell values, age, sex, iris color, and cataract type between patients with no surface LECs and those with these cells.

At 3 months postoperatively, 23 patients (77%) with hydrogel IOLs had LECs in the anterior surface of their optics compared with 4 (10%) with PMMA IOLs and 2 (7%) with silicone IOLs ($P = .001$). These patients with hydrogel IOLs who had LECs at 3 months were found to have significantly lower anterior chamber flare and cell values than those patients without LECs ($P < .001$). Similarly, the anterior chamber cell readings were significantly lower for the patients with hydrogel IOLs with LECs than those without LECs on the lens surface ($P < .001$).

In comparison, for PMMA IOLs, the average overall flare for patients with LECs was not significantly different than that for those without LECs (10.3 vs 12.2, $P = .67$), but the patients with LECs had significantly lower anterior chamber cell counts (0.59 vs 2.44, $P = .02$). No significant differences were found in the silicone group between the patients with LECs and those without.

Patients with hydrogel IOLs who had surface LECs had lower epithelioid cell reactions, with no epithelioid cells at any time, compared with 3 (7%) of 42 patient visits showing epithelioid cells for those without LECs ($P = .002$). Anterior surface small cells were seen in 22 (16%) of 135 visits of patients with LECs compared with 11 (26%) of 42 visits of patients without LECs ($P = .15$). No significant differences were found in the silicone and PMMA IOL groups between the patients with LECs and those without.

Average phacoemulsification time for the patients with LECs was 1.84 minutes compared with 1.95 minutes for patients without LECs ($P = .50$). Cumulative delivered phacoenergy was 0.41 for patients with LECs compared with 0.52 for patients without LECs ($P = .05$), indicating less surgical trauma for those patients who developed LECs.

Patients with hydrogel IOLs who had LECs, therefore, showed evidence of lower anterior chamber flare and cells postoperatively and less surgical trauma, indicating that these patients had less BAB damage postoperatively. In comparison, those patients who did not develop LECs had more inflammatory cells on the implant surface.

**COMMENT**

All IOL implants in this study gave good results in normal eyes, but hydrogel IOLs showed an enhanced response to LECs that grow over the anterior surface to a much greater extent and in a completely different pattern than that seen with PMMA and silicone IOL implants. Patients with PMMA and silicone IOLs get relatively few LECs on their anterior surfaces. These occur adjacent to the capsule rim soon after surgery, probably due to migration from the capsule edge, and...
regress over 3 months, leaving a clear margin. Conversely, in the first 1 to 3 months after surgery, patients with hydrogel IOLs tend to develop many more LECs, which are still present in a stable pattern at 1 year. They form a confluent layer with a scalloped edge mirroring the capsulorhexis contour (Figure 6) in a pattern that, in our experience, is unique to this implant. In some areas, nuclei can be seen (Figure 8). In none of the patients studied did this layer cover the central visual axis.

Seventy-seven percent of patients with hydrogel IOLs had surface LECs at 3 months after surgery compared with 10% of those with PMMA IOLs and 7% of those with silicone IOLs. We looked for reasons why some of the patients with hydrogel IOLs did not develop LECs. There was no significant difference in the preoperative flare and cell values, age, sex, iris color, and cataract type between these 2 groups. Those patients with surface LECs had significantly lower anterior chamber flare and cell values after surgery, representing less postoperative BAB damage than those in whom LECs were not present on the lens surface. Anterior chamber flare and cell readings after surgery are largely a reflection of surgical technique and trauma,

This is because fewer molecular interactions occur between hydrophilic material surfaces and the biological environment of cells. Hydrophilic surfaces demonstrate a reduced activation of granulocytes and cell adhesion to the lens surface, which is thought to be responsible for the onset of the inflammatory reaction. The patients with hydrogel IOLs studied show a reciprocal relationship between LECs and inflammatory cell attachment on the IOL surface and postoperative BAB damage, with those patients with LECs having lower flare and fewer inflammatory cells on the IOL, whereas those with no LECs having higher flare and more inflammatory cells.

Increased biocompatibility has always been considered to be beneficial, but herein is an example of a situation in which reduced breakdown of the BAB is associated with the growth of LEC sheets over the implant, indicating these IOLs may be “too biocompatible.” The functional consequences of anterior surface LECs are as yet unclear. In the patients studied, the acuity or contrast sensitivity was not affected as the LECs did not cover the visual axis. On the posterior capsule, LECs undergo proliferation and fibrous metaplasia to produce PCO. Intraocular lenses that are associated with an increased anterior surface LEC response could be anticipated to have worse PCO and, indeed, we have found hydrogel IOLs to develop significantly more PCO compared with PMMA and silicone IOLs.

The explanation for these clinical observations is likely to lie in the surface biofilm of the IOL. Any foreign material that is implanted into the body is coated with a proteinaceous biofilm within hours of surgery, and IOLs are no exception. Kochounian et al studied the biofilm of rabbit eyes, and we have shown differences in protein deposition on different IOL materials. Biofilms are highly complex structures. While they reflect protein composition and concentration in the surrounding aqueous media, proteins may be bound differentially and their biochemical properties may be changed on adsorption by denaturation or polarization. Furthermore, a biofilm is a dynamic structure with protein turnover through desorption and adsorption.

We postulate that the degree of postoperative BAB breakdown influences the composition of the biofilm on hydrogel IOLs. Comparatively low degrees of BAB damage favor LEC attachment to the lens surface, whereas higher degrees are less favorable to LECs and more favorable to inflammatory cells. Tassignon et al reported that the type of PCO is related to the degree of postoperative BAB damage. They found that eyes of patients with increased BAB damage (from diabetes or uveitis) tended to get a fibrotic pattern of PCO, whereas normal eyes tended to get Elschnig pearl formation. In conclusion, this study shows that there are significant differences between the inflammatory macrophage response and the LEC reaction with the 3 IOL types. Hydrogel IOLs were associated with a lower inflammatory cell reaction but had more LECs on their anterior surface. Those hydrogel IOLs that were associated with increased BAB damage did not develop LECs. If an IOL is biocompatible, then it may incite the growth of LECs over its surfaces, which could be disadvantageous.

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From the Archives of the ARCHIVES

Hilbert reports that his seven-year-old daughter associates the taste of good milk with the color yellow, unpleasant tastes with the color brown, and very disagreeable tastes with gray or black.