Influence of Elevated Intraocular Pressure on the Posterior Chamber–Anterior Hyaloid Membrane Barrier During Cataract Operations

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Objective: To investigate the influence of elevated intraocular pressure on the posterior chamber–anterior hyaloid membrane (PC-AHM) barrier during cataract operations in ex vivo porcine eyes.

Methods: A pressure transducer was connected to porcine eye anterior chambers (ACs). In experiment 1, ACs were perfused for 20 seconds with balanced salt solution containing 1.0-µm fluorescein beads (10 eyes per bottle height: 45, 85, 145, and 285 cm). In experiment 2, 5 ophthalmic viscosurgical devices with different molecular weights and sodium hyaluronate concentrations were infused into the ACs (20 eyes per ophthalmic viscosurgical device). After continuous curvilinear capsulorhexis, hydrodissection was performed. After both experiments, PC-AHM barrier staining was evaluated through the Miyake-Apple view.

Results: Types of fluorescein staining patterns were classified as AC, zonule of Zinn, AHM, AHM tear, and ruptured capsule. In experiment 1, plateau intraocular pressure and staining type were positively correlated (Spearman rank correlation; r = 0.703, P < .001). In experiment 2, mean peak intraocular pressure was significantly greater in the ruptured capsule–type eyes than in the AC–, zonule of Zinn–, AHM (P < .001), or AHM-tear– (P = .02) type eyes, as well as in the AHM- and AHM-tear–type eyes compared with the AC and zonule of Zinn type eyes (P < .001). Intraocular pressure was significantly higher in eyes infused with ophthalmic viscosurgical devices with a higher molecular weight or sodium hyaluronate concentration (P < .05).

Conclusions: Stress on the PC-AHM barrier increases as intraocular pressure increases. Ophthalmic viscosurgical devices with a higher molecular weight or sodium hyaluronate concentration might induce increased IOP during cataract operations.

Clinical Relevance: To maintain normal PC-AHM barrier function, excessive intraocular pressure should be avoided during cataract operations.

effect of 2 factors on the integrity of the PC-AHM barrier in isolated porcine eyes: perfusion pressure and increases in IOP during hydrodissection in ACs filled with OVDs.

**METHODS**

Porcine eyes were selected as previously reported and examined with a slitlamp microscope. Eyes with corneal trauma or other obvious abnormalities were not used.

**EXPERIMENT 1**

The effects of the pressure exerted on the PC-AHM barrier by intraocular perfusion were investigated. To monitor the IOP, a 16-gauge needle attached to a pressure sensor (DI-151RS; DATAQ Instruments, Inc., Akron, Ohio) was introduced into the AC at the 9-o’clock position of the cornea 1.5 mm inside the limbus. A closed-eye condition was maintained, and there was no leakage of the infusion fluid from the 16-gauge needle or pressure sensor.

A 27-gauge needle was attached to a bottle containing perfusion fluid consisting of balanced salt solution (BSS Plus; Alcon Laboratories, Fort Worth, Texas) and 1.0-µm fluorescein bead solution (Fluoresbrite Carboxylate YG 1.0-µm Microspheres; Polysciences Inc, Warrington, Pennsylvania) at a ratio of 100:3.0 mL. The 27-gauge needle was introduced into the AC at the 12-o’clock position of the cornea. Each eye was perfused for 20 seconds, using bottle heights of 45, 85, 145, and 285 cm. Ten eyes were tested at each height.

At the end of the perfusion, when the 27-gauge needle was removed, IOP returned to a normal level after 4 to 5 seconds in most eyes, with continuous leakage from the wound. Any IOP that remained relatively high was allowed to return to a normal level before the 16-gauge needle was removed. As a result, the AC did not collapse.

After the procedure, the eyes were cut horizontally at the equatorial region using a razor blade; the fluorescein staining of the zonule of Zinn, ciliary body, AHM, and vitreous cavity was then examined by ophthalmic surgical microscope via the Miyake-Apple view and videotaped (camera: DXC-C33; Sony Corp, Tokyo, Japan; lens: ML-0310VF; Moritex Corp, Tokyo).

**EXPERIMENT 2**

The influence of the pressure exerted on the PC-AHM barrier during hydrodissection was investigated. A 2.8-mm corneal incision was made at the 12-o’clock position in the porcine eyes, and 0.4 mL of a viscoelastic substance was infused into the AC. Four types of OVDs with different MWs and concentrations of sodium hyaluronate were tested: a very low-viscosity dispersive OVD (OVD-A: MW, 600,000 to approximately 1,200,000 Da; 10 mg/mL), a medium-viscosity dispersive OVD (OVD-B: MW, 1,530,000-2,130,000 Da; 10 mg/mL), a viscous cohesive OVD (OVD-C: MW, 1,900,000-3,900,000 Da; 10 mg/mL), and a viscoadhesive OVD (OVD-D: MW, approximately 4,000,000 Da; 23 mg/mL). In addition, 1 medium-viscosity dispersive OVD (OVD-E) containing 30 mg/mL of hyaluronate and 40 mg/mL of chondroitin sulfate was used. The MW of hyaluronate in OVD-E was 500,000 Da. After infusing the OVDs, a continuous curvilinear capsulorrhesis was made, with an average diameter of 6.5 mm.

As in experiment 1, a 16-gauge needle attached to a pressure sensor was inserted through the peripheral cornea at the 9-o’clock position. Hydrodissection was then performed (Nagahara cannula; ASICO Ltd, Westmont, Illinois). The cannula was inserted under the anterior capsule at the 6-o’clock position, contralateral to the corneal incision, and a mixture of fluorescein bead solution and balanced salt solution was rapidly infused at a rate of 3.0 mL per 10 seconds. Hydrodissection was performed by a surgeon (S.K.) who had no knowledge of which OVD had been used. The experiment was conducted on 20 eyes with each OVD and, immediately after the hydrodissection, the eyes were enucleated and examined as in experiment 1.

**STATISTICAL ANALYSES**

Spearman rank correlation tests were used to determine whether a significant correlation existed between IOP and the staining type, a measure of AHM impairment. The Jonckheere trend test was used to investigate these trends in more detail. Analysis of variance (ANOVA) was used for comparisons between multiple groups; when a significant difference was found by ANOVA (P < .05), the Tukey-Kramer multiple comparison test was performed. Data are given as mean (SD) unless otherwise indicated.

**RESULTS**

**EXPERIMENT 1: EFFECT OF PERFUSION PRESSURE ON THE PC-AHM BARRIER**

Classification of Staining Patterns Observed via Miyake-Apple View

The fluorescein bead staining patterns of the zonule of Zinn, ciliary body, AHM, and vitreous cavity were characterized using the Miyake-Apple view and videotaped (camera: DXC-C33; Sony Corp, Tokyo, Japan; lens: ML-0310VF; Moritex Corp, Tokyo).

The fluorescein bead staining patterns of the zonule of Zinn, ciliary body, AHM, and vitreous cavity were observed via the Miyake-Apple view. The fluorescein beads were observed via the Miyake-Apple view, classified into 4 types: the AC, zonule of Zinn (Zinn), AHM, and AHM tear (AHT). The AC type was designated as a staining pattern in which fluorescein beads remained in the AC (Figure 1A). When the fluorescein beads reached the zonule of Zinn, such eyes were classified as the Zinn type (Figure 1B). Eyes in which the fluorescein beads reached the space between the zonule of Zinn and the AHM were classified as the AHM type (Figure 1C); eyes in which fluorescein beads reached the AHM were classified as the AHT type (Figure 1D). Formation of an AHM tear was visually confirmed at the time of dissection.

Eyes were also examined by scanning electron microscopy. In the AC-type eyes, a small number of fluorescein beads were found in the zonule of Zinn (Figure 1E) and almost no beads were found in the ciliary body (Figure 1I). In Zinn-type eyes, a large number of fluorescein beads were present in the zonule of Zinn (Figure 1F), but almost no beads were seen in the ciliary body (Figure 1J). In AHM-type eyes, many fluorescein beads were present in both the zonule of Zinn (Figure 1G) and the ciliary body (Figure 1K). In AHT-type eyes, the zonule of Zinn was partially damaged near the AHM tear (Figure 1H). Because beads were found mostly in the torn portions of the zonule of Zinn, the damage was thought to have occurred during hydrodissection rather than during processing of the samples.

The degree of penetration of fluorescein beads was designated as grade 1 to grade 4 based on the staining patterns and scanning electron microscopic findings. A higher grade indicated deeper penetration of the fluorescein beads.
in the posterior direction. Schematic figures for each staining grade are as follows: grade 1, AC type (Figure 1M); grade 2, Zinn type (Figure 1N); grade 3, AHM type (Figure 1O); and grade 4, AHT type (Figure 1P).

**Figure 1.** Miyake-Apple view images (A-D), scanning electron microscopy of the zonule of Zinn (E-H) and ciliary body (I-L), and schematic diagrams of staining patterns (M-P). The anterior chamber→ (A, E, I, and M), zonule of Zinn→ (B, F, J, and N), anterior hyaloid membrane→ (C, G, K, and O), and anterior hyaloid membrane tear→ (D, H, L, and P) type eyes. While arrowheads in H indicate tears in the anterior hyaloid membrane→type eyes.

### Relationship Between Bottle Height and IOP

The IOP values determined during perfusion at each bottle height are shown in **Figure 2**. The IOP was highest at a bottle height of 285 cm, followed by 145, 85, and 45 cm (all \( P < .001 \), Tukey-Kramer multiple comparison test).

**Figure 2.** Plateau intraocular pressures (A, 32.28; B, 52.23; C, 102.58; and D, 199.09 mm Hg) were reached after 18.0 seconds (A), 16.1 seconds (B), 13.5 seconds (C), and 9.9 seconds (D) for bottle heights of 45, 85, 145, and 285 cm, respectively. Black arrows indicate the start of perfusion.

The mean (SD) plateau IOPs were 30.00 (2.59) mm Hg at a bottle height of 45 cm, 56.12 (3.73) mm Hg at 85 cm, 105.72 (3.91) mm Hg at 145 cm, and 210.51 (15.34) mm Hg at 285 cm. The differences in the plateau IOPs of the 4 groups were statistically significant (\( P < .001 \), ANOVA). The IOP began to increase when perfusion began and reached a plateau at a time that varied depending on the bottle height. The times required for the IOP to reach a plateau at each bottle height were 17.8 (0.8) seconds for a height of 45 cm, 16.6 (0.7) seconds for 85 cm, 13.8 (1.2) seconds for 145 cm, and 10.1 (1.0) seconds for 285 cm.
The differences in the time required for each group to reach the plateau IOP were significant ($P < .001$, ANOVA). The 45-cm group took the longest time to reach the plateau IOP, followed by the 85-cm group ($P = .04$), 145-cm group ($P < .001$), and 285-cm group ($P < .001$, Tukey-Kramer multiple comparison test).

**Relationship Between IOP and Staining Pattern**

The relationship between the plateau IOP and the staining pattern seen at each bottle height is given in **Table 1**. A significant correlation was found between plateau IOP and the staining grade (Spearman rank correlation; $r = 0.703, P < .001$). The Jonckheere trend test indicated that the staining grade became significantly higher as IOP increased ($P < .001$). Moreover, a significant difference was found among the plateau IOPs of the 4 types of eyes ($P = .001$, ANOVA); the plateau IOP in the AC-type eyes was significantly lower than that in the AHM-type eyes ($P = .01$, Tukey-Kramer multiple comparison test) and the AHT-type eyes ($P = .003$, Tukey-Kramer multiple comparison test). The plateau IOP in Zinn-type eyes was significantly lower than that in AHT-type eyes ($P = .04$, Tukey-Kramer multiple comparison test).

**EXPERIMENT 2: EFFECT OF HYDRODISSECTION ON THE PC-AHM BARRIER**

**Classification of Staining Patterns Following Hydrodissection**

The 4 types of staining patterns designated in experiment 1 were also observed after hydrodissection was performed in experiment 2. In addition, a new staining pattern was recognized in which the posterior lens capsule was ruptured. This was designated as the rupture type and was not assigned a numeric grade because the rupture occurred in an anatomically distant site, independent of bead penetration. Typical examples of each staining pattern are shown in **Figure 3**.
Relationship Between Staining Pattern and Peak IOP During Hydrodissection Performed With Each OVD

Staining types and peak IOP values observed during hydrodissection with each OVD are summarized in Table 2. Representative graphs of the change in IOP during hydrodissection with each type of OVD are shown in Figure 4. When OVD-A or OVD-B was used, the mean peak IOPs were only slightly elevated to 15.49 (12.42) mm Hg and 21.08 (8.90) mm Hg, respectively. In contrast, when OVD-C, OVD-D, or OVD-E was used, the IOP increased to mean peak values of 40.96 (33.20) mm Hg, 115.33 (64.92) mm Hg, and 56.08 (47.85) mm Hg, respectively, within 2 seconds after hydrodissection was initiated.

No significant differences were found among the 5 groups in the amount of balanced salt solution required for hydrodissection ($P = .47$, ANOVA) or the IOP before hydrodissection ($P = .34$, ANOVA); however, there was a significant difference among the groups with regard to the peak IOP recorded during hydrodissection ($P < .001$, ANOVA). A significantly higher peak IOP value was found in the OVD-D group compared with the other OVD groups ($P < .001$, Tukey-Kramer multiple comparison test). In addition, the peak IOP value in the OVD-E group was significantly higher than that in either the OVD-A group ($P = .01$, Tukey-Kramer multiple comparison test) or the OVD-B group ($P = .048$, Tukey-Kramer multiple comparison test).

Relationship Between Peak IOP and Staining Pattern

The mean peak IOPs among the staining patterns were 21.19 (11.91) mm Hg (range, 4.03-50.61 mm Hg) for the AC-type eyes, 29.76 (15.91) mm Hg (range, 3.81-57.50 mm Hg) for the Zinn-type eyes, 86.59 (60.31) mm Hg (range, 16.21-245.62 mm Hg) for the AHM-type eyes, 122.47 (43.41) mm Hg (range, 75.18-211.48 mm Hg) for the AHT-type eyes, and 189.47 (40.82) mm Hg (range, 142.42-215.38 mm Hg) for the rupture-type eyes.

A significant difference was found among the peak IOP values of the 5 staining types ($P < .001$, ANOVA). The peak IOP in rupture-type eyes was significantly greater than in AC- ($P < .001$), Zinn- ($P < .001$), AHM- ($P < .001$), or AHT- ($P = .02$) type eyes. Moreover, the peak IOP for AHT-type eyes was significantly greater than that of the AC- ($P < .001$) or Zinn- ($P < .001$) type eyes, and the peak IOP for AHM-type eyes was also significantly higher than that of the AC- ($P < .001$) or Zinn- ($P < .001$) type eyes (all Tukey-Kramer multiple comparison test).

Table 2. Staining Types and Peak IOP During Hydrodissection Performed With Each Viscoelastic Substancea

<table>
<thead>
<tr>
<th>OVD</th>
<th>Amount of BSS injected, mL</th>
<th>Initial IOP, mm Hg</th>
<th>Peak IOP, mm Hg</th>
<th>Staining type, No. of eyesb</th>
</tr>
</thead>
<tbody>
<tr>
<td>OVD-A</td>
<td>1.38 (0.79)</td>
<td>3.58 (1.61)</td>
<td>15.49 (12.42)</td>
<td>AC 16</td>
</tr>
<tr>
<td>OVD-B</td>
<td>1.29 (0.83)</td>
<td>4.28 (1.91)</td>
<td>21.08 (8.90)</td>
<td>Zinn 4</td>
</tr>
<tr>
<td>OVD-C</td>
<td>1.05 (0.67)</td>
<td>4.24 (1.25)</td>
<td>40.96 (33.20)</td>
<td>AHM 0</td>
</tr>
<tr>
<td>OVD-D</td>
<td>1.50 (1.02)</td>
<td>4.25 (1.33)</td>
<td>115.33 (64.92)</td>
<td>AHT 0</td>
</tr>
<tr>
<td>OVD-E</td>
<td>1.45 (1.02)</td>
<td>3.61 (1.34)</td>
<td>56.08 (47.85)</td>
<td>Rupture 0</td>
</tr>
</tbody>
</table>

Abbreviations: AC, anterior chamber; AHM, anterior hyaloid membrane; AHT, anterior hyaloid membrane tear; BSS, balanced salt solution; ellipses, not calculated for the staining types; IOP, intraocular pressure; OVD, ophthalmic viscosurgical device; rupture, ruptured capsule; Zinn, zonule of Zinn.

*Values are expressed as mean (SD) unless otherwise indicated.

b Tukey-Kramer multiple comparison test.

c Each group included 20 eyes.

Figure 4. Increase in intraocular pressure during hydrodissection. Black arrows indicate start of hydrodissection. White arrows indicate peak intraocular pressure: 16.21 mm Hg (A), 19.47 mm Hg (B), 38.48 mm Hg (C), 137.80 mm Hg (D), and 56.06 mm Hg (E).
A significant correlation was found between mean peak IOP and the staining grade (Spearman rank correlation; $r=0.706, P<.001$) and, as in the perfusion pressure experiment, the staining grade became significantly higher as IOP increased.

**COMMENT**

As modern cataract repair evolved into a sophisticated closed-eye procedure, critical new surgical techniques were integrated. Some of these techniques, such as hydrodissection and lens nucleus processing, are accompanied by increases in IOP. Because it is difficult to evaluate the effect of increased IOP during these procedures, especially on the PC-AHM barrier, little information has been gathered. However, by using fluorescein beads and porcine eyes, we were able to demonstrate that, as IOP increases, the PC-AHM barrier is exposed to increasingly larger amounts of pressure. Observation of fluorescein bead staining via the Miyake-Apple view allowed us to identify 5 different staining patterns: AC, Zinn, AHM, AHT, and rupture types, listed from the type experiencing the lowest pressure to that experiencing the highest pressure. Among these patterns, the AHT and rupture types are dangerous in terms of vitreous contamination because the PC-AHM barrier has broken down in these situations.

Previous studies have demonstrated that hydrodissection produces large increases in IOP and damage to the zonule of Zinn or posterior capsule. For example, Khng et al. reported that IOP during hydrodissection ranged from 78.6 mm Hg to 223.2 mm Hg in 4 human cadaver eyes, and Ohnuma et al. reported that it increased up to 170.9 mm Hg in porcine eyes. In this study, we also demonstrated that AHM tears and even ruptures of the posterior capsule are prone to occur owing to excessive increases in IOP. Scanning electron microscopy showed that tear formation in the AHM (Figure 1H) was associated with damage to the corresponding portion of the zonule of Zinn in AHT-type eyes, indicating that this region experienced a high amount of pressure. Our results indicate that eyes subjected to pressure higher than 75 mm Hg during hydrodissection are at increased risk for AHM tears, and those subjected to pressure higher than 140 mm Hg are at greater risk for posterior capsule rupture, emphasizing the importance of monitoring IOP in clinical practice, especially during hydrodissection.

Our study also showed that the magnitude of increase in IOP during hydrodissection varied widely depending on the type of OVD used. During cataract operations, the OVD plays a role in maintaining a surgical space in which continuous curvilinear capsulorhexis can be performed and the intraocular lens can be inserted. The OVD also protects the corneal endothelium. Recently, OVDs with different properties have been developed to accommodate a variety of clinical situations. 

Previous studies have found that IOP tends to increase more easily when a viscoadaptive OVD (OVD-D) is used during hydrodissection. Similarly, the OVD-D and the medium-viscosity dispersive OVD (OVD-E) were associated with significantly higher increases in IOP in the postoperative period. This suggests that it is more difficult for these OVDs to leave the eye. Because OVDs with higher concentrations of sodium hyaluronate and high MW are less likely to leak from the AC during surgical manipulation, careless maneuvers may lead to failure of the PC-AHM barrier, as shown in the OVD-D or OVD-E groups. When such OVDs are used, it is necessary to avoid sealing the wound during hydrodissection. In contrast, when using very low- or medium-viscosity dispersive OVDs, such as OVD-A and OVD-B, there is little need to watch for rises in IOP. Thus, as minimal-incision cataract operations become more widespread, the space-occupying effect of OVDs should become less of a priority and a different strategy for choosing OVDs may be warranted in general cataract cases.

It is well known that the Miyake-Apple view is useful for examining the effects of surgical manipulations of the lens capsule and the zonule of Zinn during cataract operations. This technique allows the researcher to observe movements of these structures that cannot be seen by the surgeon during nucleus separation or intraocular lens insertion. As shown in this study, this technique, combined with fluorescein bead perfusion, offers a new approach for evaluating the effect of IOP on the PC-AHM barrier.

Because the fluorescein beads used in this study were 1.0 µm in diameter, similar in size to bacteria, distribution of the beads may mimic bacterial contamination. For instance, in AC- or Zinn-type eyes, bacterial contamination would be expected to remain within the AC, the capsule, or the zonule of Zinn. The 3-layered zonule of Zinn forms a tightly organized meshwork over the posterior chamber and acts as a filter to prevent further bacterial invasion. However, in the current study, because the eye was exposed to higher amounts of pressure, the beads were prone to slip through the zonule of Zinn and approach the AHM. Under conditions of higher pressure, the fluorescein beads either filled the posterior cavity or spread into the vitreous cavity through a tear formed in the AHM. Because formation of AHM tears offers a direct path to the vitreous cavity, these tears may be an important risk factor for endophthalmitis, equal to the risk with posterior capsule rupture. We assume that AHM tears may be one of the predisposing factors for postoperative endophthalmitis in eyes that underwent a seemingly uneventful operation.

This study has some limitations. First, although the general trends observed in porcine eyes are probably similar to those in humans, the IOP changes observed in our model may not exactly reflect the changes in human eyes because of the absence of aqueous flow. Second, the anatomic structure of the anterior segment, especially the zonule of Zinn, is similar to that of a human eye, but the integrity of the tissue may be weakened in an enucleated porcine eye. Third, we performed hydrodissection by rapidly injecting balanced salt solution into the AC to examine the effect of increased IOP on the integrity of the PC-AHM barrier in experimental conditions. However, in clinical situations, breakdown of the PC-AHM barrier does not occur at such a high rate because, in most cases, surgeons release the OVD from the AC during hydrodissection to avoid unnecessary IOP elevation.

In conclusion, use of OVDs with higher MWs or higher concentrations of sodium hyaluronate predisposes the eye...
to an increased risk of PC-AHM impairment during hydrodissection. Although AHM tears or rupture of the posterior capsule may be infrequent in the clinical setting, our study shows that breakdown of the PC-AHM barrier is possible any time that IOP increases significantly, potentially leading to postoperative endophthalmitis following an otherwise uneventful operation. Thus, surgeons should carefully monitor IOP during cataract operations.

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