Anterior and Posterior Axial Lens Displacement and Human Aqueous Outflow Facility

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We studied the effect of anterior and posterior axial crystalline lens displacement (and thereby ciliary tone) on the aqueous humor outflow facility in enucleated human eyes. After attaching a reversible footplate plunger to the anterior lens capsule with cyanoacrylate, the lens was placed in one of three positions: "neutral baseline," posterior displacement (2.5 mm), or anterior displacement (2.0 mm). In seven pairs of eyes, the mean "neutral baseline" was not statistically different from the control eye, but anterior lens displacement decreased outflow facility “C” by 0.14 (36%) (P < 0.0001), and posterior displacement increased “C” by 0.18 (50%) (P < 0.01). Anterior or posterior lens displacement after complete ciliary body detachment produced no effect on outflow facility in two pairs. Histologic correlation studies demonstrated narrowing of the intertrabecular spaces and Schlemm’s canal in the eyes fixed in anterior lens displacement, and widening of the same structures in the eyes fixed in posterior lens displacement. The lens-zonular-ciliotrabecular force vectors are responsible for the compression or decompression of the meshwork and Schlemm’s canal in this model, with compression decreasing, and decompression increasing aqueous humor outflow facility. Invest Ophthalmol Vis Sci 29:1159-1164, 1988

In early quantitative anterior chamber perfusion experiments, inconsistent results were obtained when the relationship between the intraocular perfusion pressure and the facility of aqueous humor outflow was studied. However, Ellingsen, Grant1 and others recognized that when perfusate was introduced into the anterior chamber, a reverse pupillary block occurred, so that the pupillary border acted as a valve against the lens, thereby inhibiting flow into the posterior chamber. Accompanying this reverse pupillary block was an artificial deepening of the anterior chamber, posteriorly displacing the lens-iris diaphragm, most pronounced at elevated perfusion pressures. When reverse pupillary block was eliminated by an iridotomy or placement of the perfusion needle into the posterior chamber, the chamber-deepening effect was minimized, and a consistent relationship between the perfusion pressure and the outflow facility became apparent. While elevated perfusion pressure in the absence of reverse pupillary block decreased outflow facility in a reversible fashion, the artifactitious anterior chamber-deepening effect accompanying the reverse pupillary block had tended to counteract this influence, creating discrepancies in results.

Using these observations, Van Buskirk and Grant2,3 further studied the effect of posterior lens displacement in an attempt to develop forces on the ciliary body and trabecular meshwork simulating cyclotonia. A hydraulically driven footplate placed through the center of a Grant corneal fitting produced posterior lens displacement (lens depression) in a controlled fashion. This caused a reversible increase in outflow facility, which was correlated with a widening of the trabecular meshwork and increased diameter of Schlemm’s Canal histologically.4 Moses obtained similar results in related experiments.5 Since posterior lens displacement is known to increase aqueous outflow facility, we hypothesized that anterior lens displacement might have the opposite effect, decreasing outflow facility. To further study effects of manipulations of ciliary tone on aqueous humor outflow facility, a technique was developed in which a footplate similar to that used by Van Buskirk2 could be attached to the anterior lens capsule by cyanoacrylate adhesive. This allowed alteration of ciliary muscle forces by inducing changes in lens position in either an anterior or posterior direction. A reversible screw-driven metered footplate plunger, capable of measuring footplate excursions in increments of 0.1 mm, was employed to precisely control
the position of the lens, while allowing simultaneous monitoring of outflow facility.

Materials and Methods

Nine pairs of ostensibly normal human adult cadaver eyes, enucleated within 4 hr of demise and refrigerated in a moist chamber, were perfused within 48 hr of death. After a central 4.5 mm corneal trephination, a radial iridotomy was performed to the peripheral iris, followed by total iridectomy by gentle traction. The anterior chamber was then irrigated with perfusate to remove liberated pigment or debris from the prior manipulations. After drying the anterior chamber with cellulose sponges, the integrity of the lens capsule and zonules was confirmed with inspection, and the anterior chamber depth noted. A 3–4 mm diameter application of cyanoacrylate adhesive was placed as a thin layer on the central anterior lens capsule and allowed to partially dry for about 1 min. The lens footplate was then introduced into the anterior chamber through the trephine orifice, in an extended position. Then, prior to any footplate-lens contact, the footplate was retracted to a position of 2.0 mm clearance between the footplate and the inferior plate of the Grant corneal fitting. Next, the inferior plate of the Grant fitting was placed into the air-filled anterior chamber, and the fitting secured. To facilitate formation of a secure adhesion between the footplate and lens capsule, the footplate was extended to 4.5 mm footplate-corneal distance to gently compress the footplate against the lens capsule. The anterior chamber was allowed to remain dry for about 5 min to further promote adhesion, since preliminary experience indicated that a brief drying period was necessary to promote adequate footplate-lens adhesion. The anterior chamber was next filled with perfusate, and any bubbles arising at the glue-fluid interface were removed or collapsed with a 30-gauge needle on a syringe. The “neutral position” of 3.0 mm lens-corneal distance was achieved, and perfusion was begun. The 3.0 mm baseline was derived from data of Van Buskirk and Moses, and on our own observations of the chamber depth in these excised eyes, and did not appear to appreciably distort the normal lens position. Constant pressure perfusion at 15 mm Hg at 22°C, was employed, using Dulbecco’s PO₄-buffered saline augmented with 5.5 mM glucose.

The control eye received identical trephination, iridectomy, and irrigation, and the anterior chamber was allowed to remain dry for a period comparable to the experimental eye. Assignment to experimental versus control eyes within the pairs was randomized. Beginning with the experimental eye in the 3.0 mm corneal-lens distance “baseline” position, the eyes were perfused for 1 hr to achieve steady-state conditions before the initial outflow facilities were recorded. Following the baseline determinations, a series of manipulations were performed in a set sequence. After each manipulation, 15 min elapsed before a 5 min facility measurement was obtained for each eye. In the first manipulation, the footplate was extended 2.5 mm to a 5.5 mm lens-corneal distance, posteriorly displacing the lens. After facility measurements were obtained, the footplate was returned to the 3.0 mm neutral baseline position. Next, the footplate was retracted an additional 2.0 mm, creating a 1.0 mm lens-corneal distance. Following a second return to the neutral baseline position, the footplate was again extended to the 5.5 mm position, as a test of the reversibility of the procedure. At the conclusion of the experiments, the eyes were either dissected to demonstrate adequate footplate-lens adhesion, an intact lens capsule, and the absence of zonular rupture or inadvertent spread of the adhesive into the chamber angle, or were fixed at flow and pressure with 3% gluteraldehyde with 1% Na cacodylate buffer. The fixed eyes were also inspected later during removal from the apparatus. Seven pairs of eyes were perfused according to this protocol.

In addition, two pairs of eyes were perfused using the identical perfusion protocol, except that the experimental eye additionally received a 360° disinsertion of the ciliary body by sharp dissection with a Swan goniotomy knife via the central trephine prior to placing the apparatus into the anterior chamber. The incision was located just posterior to the scleral spur.

The experimental design allowed comparison of the experimental eye not only with the unmanipulated fellow eye, but also with its own neutral baseline position before and after each manipulation. All results are reported in terms of outflow facility “C,” the units of which are μl/min mm Hg. Statistical analysis was performed using a two-tailed t-test.

Results

The mean initial baseline facilities were slightly lower for the experimental eyes, but this small difference was not statistically significant (Table 1). The mean facilities for the control eyes were quite stable during the duration of the experiments. After posterior displacement of the lens 2.5 mm, the mean facility of the experimental eyes increased significantly, returning toward the prior baseline upon resumption of the neutral position (Table 1, Fig. 1). Subsequent anterior lens displacement of 2.0 mm decreased the mean facility significantly, but return to the baseline position resulted in an increase in facility, again qual-
Table 1. Comparison of experimental eyes to their own most recent baseline position, accounting for any drift in control eyes

<table>
<thead>
<tr>
<th>Position</th>
<th>C_{exp} ± SEM</th>
<th>C_{cont} ± SEM</th>
<th>Difference between current C_{exp} and most recent baseline C_{exp}</th>
<th>Statistical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial baseline</td>
<td>0.36 ± 0.04</td>
<td>0.40 ± 0.04</td>
<td>+0.18 ± 0.04</td>
<td>+50% P &lt; 0.01</td>
</tr>
<tr>
<td>Posterior lens</td>
<td>0.52 ± 0.06</td>
<td>0.38 ± 0.04</td>
<td>-0.14 ± 0.01</td>
<td>-36% P &lt; 0.0001</td>
</tr>
<tr>
<td>Displacement 2.5 mm #1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline #2</td>
<td>0.39 ± 0.03</td>
<td>0.38 ± 0.04</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior lens</td>
<td>0.27 ± 0.02</td>
<td>0.40 ± 0.04</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Displacement 2.0 mm</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline #3</td>
<td>0.32 ± 0.03</td>
<td>0.39 ± 0.04</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Posterior lens</td>
<td>0.43 ± 0.05</td>
<td>0.41 ± 0.04</td>
<td>+0.09 ± 0.03</td>
<td>+28% P &lt; 0.05</td>
</tr>
<tr>
<td>Displacement 2.5 mm #2</td>
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* See text.

This allowed the experimental eye to be compared not only with the unmanipulated fellow eye, but also to its own most recent baseline position.

The two pairs of eyes perfused with the same lens manipulations in the experimental eye, except for the addition of a 360° ciliary body detachment, demonstrated virtually no effect of lens elevation or depression on the experimental eye (Fig. 2).

Light microscopy of representative sections of eyes fixed in lens elevation or depression demonstrated relative widening of the intertrabecular spaces and Schlemm's canal in the eyes fixed in lens depression, as compared with the control eyes. The eyes fixed in lens elevation demonstrated relative narrowing of intertrabecular spaces, narrowing but not complete collapse of Schlemm's canal, and relative compactness of the ciliary muscle fibers (Figs. 3, 4).

Discussion

Our work with posterior lens displacement confirms the findings of Van Buskirk,2-4 and Moses5 on the functional and morphologic effects of lens de-
Fig. 3. Lens elevation. Ciliary muscle fibers (CB) are more compact and adjacent trabecular spaces (T) are relatively narrow. Scleral spur (S) lies against Schlemm's canal (SC) which has a small lumen. AC = anterior chamber. X285.

pression. The isolated effect of anterior lens displacement on the facility of aqueous outflow, the opposite conditions of the previously cited experiments, was especially of interest. Presuming the involvement of a mechanical mechanism, no outflow effect would be expected if inadequate vectors were generated on the aqueous outflow system. An alternate possibility with anterior lens displacement would be an increase in outflow facility as a result of nonspecific effects of zonular tension on the ciliary body and outflow system, or possibly due to the effects of manipulation alone. The third alternative would involve the reversal of the zonular-ciliotrabecular vectors operant in posterior lens displacement, which would result in a decrease in outflow facility accompanying anterior lens displacement, as was found in our study.

Previous studies by Francois, Becker, Barany, and Grant, and others had demonstrated decreased outflow facility following experimental shallowing of the anterior chamber. However, the techniques used to shallow the chamber, such as compressing the sclera at the equator, or intravitreal injections, could possibly introduce artifacts altering the very parameter under study. Additionally, some procedures offered no control over pupillary block, or even direct closure of the angle due to iris apposition. Furthermore, the extent of chamber shallowing was difficult to quantitate for correlation with the functional results. For these reasons, it seemed desirable to reconsider the question of the effect of anterior lens displacement on aqueous outflow facility.

Anterior lens displacement, produced by a technique attempting to minimize unrelated manipulation to adjacent structures, produced a reversible decrease in outflow facility, in agreement with earlier works using different techniques.

The mechanism by which both anterior and posterior lens displacement alters aqueous outflow facility presumably involves alterations in zonular tension vectors transmitted to the ciliary body and trabecular meshwork. Rohen has reported the presence of connecting fibrils from the ciliary body directly into the trabecular meshwork, which may also be placed under tension by this experimental technique. Flocks and Zweng, among others, have demonstrated a widening of intertrabecular spaces and posterior displacement of the scleral spur in pilocarpine treated monkey eyes, similar to the effect of posterior lens
displacement. The tendency of anterior lens displacement to narrow the intertrabecular spaces and Schlemm’s canal appeared similar to the effect on primate eyes treated with atropine in Flocks and Zweng’s study. We believe this is the cause of the decrease in outflow facility in the eyes in the current study. A similar process could explain the elevation of intraocular pressure in some patients following cycloplegia, despite gonioscopically open angles. The phenomenon of meshwork compression and collapse in these experiments, although mediated differently, might also explain the observations of Berson on the effect of cataract sutures in the limbal region, or postoperative pressure elevations in aphakic penetrating keratoplasty, as suggested by Olson, Kaufman and colleagues. Another possibility is that the ciliary body exerts a small tonic contraction force on the trabecular meshwork, or at least prevents meshwork compression, even in a postmortem state. When the lens is displaced forward, this force would be negated, allowing meshwork compression and narrowing of intertrabecular spaces, decreasing outflow facility.

In our study, the fact that both lens elevation and depression produced functional changes which were reversible argues against irreversible structural damage as the major mechanism operative in the experimental model presented. The total iridectomy prevented both pupillary block and appositional angle closure, and further evidence against any artifactitious pretrabecular block is the lack of effect of lens elevation when combined with ciliary detachment. Clearly the chamber depth alone has no effect on outflow facility in this model. Changes in the vectors on the ciliary body and outflow system by mechanical means are therefore capable of modulating the outflow facilities in these excised eyes.

Although this study cannot differentiate whether the decrease in outflow facility with lens elevation was related primarily to that of compression of intertrabecular spaces or changes in diameter of Schlemm’s canal, both mechanisms may have been involved.

Moses observed that lens depression and choroidal stretching are relatively inefficient means of altering aqueous outflow facility, and the comparatively large and unphysiologic lens excursions required by our experiments to produce facility changes support this concept. Nevertheless, this work, performed in a
manner designed to minimize distortion of adjacent ocular structures, confirms previous observations regarding the effect of axial lens displacements on aqueous outflow facility, and may afford opportunities to quantitatively explore additional considerations of mechanical effects on aqueous outflow function.

**Key words:** lens displacement, aqueous outflow, trabecular meshwork, trabecular compression, and ciliary tension

**References**