Increased pressure after paracentesis of the rabbit eye is completely accounted for by prostaglandin synthesis and release plus pupillary block

Abdulrahman Al-Ghadyan, Alden Mead, and Marvin Sears

Paracentesis of the anterior chamber of the rabbit eye results in hyperemia, increased protein in the aqueous, elevated intraocular pressure, and miosis. Aspirin does not affect miosis but attenuates the pressure and protein response by about 60%. Pupillary block resulting from miosis aggravates the rise in intraocular pressure after paracentesis. Iridectomy prevents 50% of the rise in intraocular pressure (as does mydriasis). Pretreatment with aspirin plus iridectomy virtually eliminates the elevation of intraocular pressure consequent to paracentesis.

Key words: paracentesis, prostaglandin, pupillary block, aspirin, intraocular pressure, iridectomy, protein

The eye of the rabbit responds to trauma and other irritants with conjunctival and iridal hyperemia, increased protein in the aqueous humor, increased intraocular pressure (IOP), and miosis. This irritative response was reviewed in 1931 and again in 1960 when an attempt was first made to separate the individual components, and more recently studies of the role of endogenous prostaglandins in the irritative response rekindled interest in the topic.

The purpose of this particular work was to evaluate the factors causing the elevated IOP after the ocular stimulus of paracentesis. Recent work has suggested that the miotic response might have a different pathway and/or mediator from the three other elements of the irritative response and also that the miosis could contribute to the pressure rise. Pupillary block is well known to occur in association with miosis in the clinical arena. Often small pupils prevent easy access of aqueous to the anterior chamber from the posterior chamber. The base of the iris bows forward, closing the angle and blocking outflow, and the IOP rises. It therefore seemed logical to study the effect of this factor by eliminating it with either iridectomy or pupillary dilation to learn the effects on the subsequent pressure rise after a standardized "irritation" by paracentesis. The results of early work by Wudka and Leopold lent credence to the hypothesis.

Methods

Intraocular pressure. Thirty albino rabbits, weighing 2 to 2.5 kg, had their IOP recorded with
Fig. 1. The figures have been normalized, so that the maximum rise in IOP after paracentesis has been set equal to 100%. Bars indicate ±1 S.E.M. All data recorded for all groups were taken at the time of maximum effect after paracentesis. (See Table I). The change in pressure from baseline in the sector iridectomy only vs. the control group is not statistically significant, but the average change in pressure in all iridectomy animals, peripheral plus sector, is significantly different from that in controls. The changes in pressure in all other groups are statistically significantly different from baseline pressures, with p < 0.01. The separate effects of iridectomy and aspirin on the pressure rise after paracentesis were of approximately the same order.

an Alcon applanation tonometer. Under general anesthesia with nembutal, 20 mg/kg intravenously, right eyes were subjected to iridectomy about 1 to 1:30 o clock in size as in Fig. 1. The rabbits were kept for a minimum of 3 weeks until no sign of inflammation was present. Rabbits with surgical complications were eliminated. The IOP was checked again in 24 rabbits of a successful group, which was divided into two groups of 12 rabbits each.

First group. Under local tetracaine anesthesia, both anterior chambers were evacuated with a 30-gauge needle in 12 rabbits after baseline pressures were recorded. Pressure was again recorded at 15, 30, 45, 60, 90, and 120 min after paracentesis.

Second group. Twelve rabbits were pretreated with 600 mg of aspirin by suppository 1 hr prior to paracentesis. The same procedure was then repeated as in the first group.

Iridectomy. Five rabbits were subjected to small right peripheral iridectomies.

dilation. Six albino rabbits, weighing 2 to 2.5 kg, had their IOP measured. The right pupil was dilated with 2.5% phenylephrine and 0.25% scopolamine until a final diameter of about 10 mm was accomplished. Paracentesis was done OU, and IOP recorded as described previously.

Protein. Twelve rabbits, weighing 2 to 2.5 kg, had right sector iridectomy. After at least 3 weeks had elapsed, these rabbits were divided into two groups of six.

First group. Six rabbits had both anterior chambers evacuated with a 30-gauge needle as described. Paracentesis was repeated after 90 min, and aqueous was collected for protein determination with the Goldberg refractometer.

Second group. Six rabbits were pretreated with 600 mg of aspirin suppository 1 hr before paracentesis. Otherwise the same procedure was repeated as in the first group.

Miosis

First group. Six rabbits, 2 to 2.5 kg, had their pupil diameters checked by infrared illumination.
Under local anesthesia with tetracaine both anterior chambers were evacuated with a 30-gauge needle. Pupil diameter was checked at 5, 15, 30, 45, and 60 min after paracentesis.

**Second group.** Six rabbits were pretreated with 600 mg of aspirin 1 hr prior to paracentesis. Pupil diameters were measured as in the first group.

**Evaluation of chamber angle.** Although slit-lamp examination was done on many of the animals, long laboratory experience with rabbits dictated the lack of success of evaluating angle closure because of extremely narrow approaches and angles in the eyes of rabbits. Thus biomicroscopy was used only to evaluate inflammation after iridectomy in order to choose the correct time to proceed with the protocol of paracentesis.

**Results**

Immediately after paracentesis the anterior chamber collapsed. The pupil constricted within 5 min, even in those eyes of animals pretreated with aspirin. Gradually the anterior chamber re-formed. The chamber re-formed more rapidly in those not pretreated with aspirin. Hyperemia and flare were observed 15 min after paracentesis but were less obvious in those rabbits pretreated with aspirin. Eyes with sector iridectomy had increased flare compared with those subjected to peripheral iridectomy. (See Fig. 1.)

**Intraocular pressure (Table I).** The pressure rise after paracentesis was highest in the control animals having no iridectomy and no aspirin pretreatment. Average pressure rose from 23.6 to 35 mm Hg and maintained this level for 2 hr. Eyes of animals with sector iridectomy had a less elevated pressure than controls. The pressure rose from 23.3 to 30 mm Hg after paracentesis. Treatment with peripheral iridectomy was somewhat more effective in reducing the pressure rise after paracentesis. In eyes of five of these animals the pressure after paracentesis rose less than 5.0 mm Hg. The area of surgical trauma involved less of the blood-aqueous barrier. Perhaps the eye with peripheral iridectomy was less vulnerable to barrier breakdown than the more traumatized eye with sector iridectomy (see Discussion). The aspirinized group also showed reduced maximum rise in IOP: 23 to 28.2 mm Hg, 45 min after paracentesis.

The final group of aspirin pretreatment plus sector iridectomy done to prevent pupillary block completely eliminated the postparacentesis elevation in IOP. Immediately after paracentesis the pressure declined from 21.9 ± 0.9 mm Hg baseline to 12.5 mm Hg and then gradually rose only to 19 ± 1.2 (Table I) 2 hr after paracentesis. Eyes with peripheral iridectomy plus aspirin responded the way eyes with sector iridectomy plus aspirin did. The pressure in the noniridectomized eyes in this aspirinized group 60 min after paracentesis was 25.3 mm Hg (8) or 3.3 mm Hg above the baseline. The average IOP of aspirinized animals in eyes with peripheral iridectomy (8) decreased immediately after paracentesis from 22.5 to 12.7 mm Hg and gradually increased only to 17.3 after 45 and 60 min.

After paracentesis eyes with dilated pupils demonstrated less elevation of IOP than the eyes with nondilated pupils. Like other controls, peak elevation of IOP in nondilated

---

**Table I. Effect of aspirin and sector iridectomy on IOP after paracentesis**

<table>
<thead>
<tr>
<th></th>
<th>Baseline IOP</th>
<th>15 min</th>
<th>30 min</th>
<th>45 min</th>
<th>60 min</th>
<th>90 min</th>
<th>120 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>LE no therapy (n = 12)</td>
<td>23.6 ± 0.5</td>
<td>35.0 ± 1.6</td>
<td>34.7 ± 0.2</td>
<td>35.6 ± 1.7*</td>
<td>34.4 ± 2.6</td>
<td>31.6 ± 1.9</td>
<td>30.8 ± 2.0</td>
</tr>
<tr>
<td>RE with iridectomy (n = 12)</td>
<td>23.3 ± 0.7</td>
<td>30.0 ± 3.0</td>
<td>29.3 ± 1.7</td>
<td>30.3 ± 1.6</td>
<td>31.9 ± 2.1*</td>
<td>26.9 ± 1.1</td>
<td>23.5 ± 1.2</td>
</tr>
<tr>
<td>RE with aspirin and iridectomy (n = 12)</td>
<td>21.9 ± 0.9</td>
<td>10.7 ± 1.4</td>
<td>11.4 ± 1.4</td>
<td>12.4 ± 1.1</td>
<td>16.6 ± 1.9</td>
<td>14.3 ± 1.7</td>
<td>19.0 ± 1.6*</td>
</tr>
<tr>
<td>LE with aspirin (n = 12)</td>
<td>23.0 ± 0.7</td>
<td>20.2 ± 3.1</td>
<td>22.9 ± 2.9</td>
<td>28.2 ± 2.7*</td>
<td>27.9 ± 2.8</td>
<td>24.9 ± 2.2</td>
<td>20.7 ± 2.7</td>
</tr>
</tbody>
</table>

IOP in 12 awake animals before surgery averaged 23.6 ± 0.5 mm Hg (mean ± S.E.M.). *Pressures used for construction of Fig. 1.
Table II. IOP in dilated and nondilated eyes after paracentesis

<table>
<thead>
<tr>
<th></th>
<th>Baseline IOP</th>
<th>15 min</th>
<th>30 min</th>
<th>45 min</th>
<th>60 min</th>
<th>90 min</th>
<th>120 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>RE, dilated (6 eyes)</td>
<td>20</td>
<td>13.0</td>
<td>22.5</td>
<td>26.0</td>
<td>27.5</td>
<td>26.5</td>
<td>21.5</td>
</tr>
<tr>
<td>LE (6 eyes)</td>
<td>24</td>
<td>35.5</td>
<td>34.1</td>
<td>34.5</td>
<td>34.0</td>
<td>33.5</td>
<td>28.0</td>
</tr>
</tbody>
</table>

Table III. Protein in the secondary aqueous of rabbits pretreated with aspirin and iridectomy

<table>
<thead>
<tr>
<th></th>
<th>No. of eyes</th>
<th>Protein level in aqueous (gm/100 ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No interference</td>
<td>6</td>
<td>4.0 ± 0.2</td>
</tr>
<tr>
<td>Iridectomy alone</td>
<td>6</td>
<td>4.4 ± 0.1</td>
</tr>
<tr>
<td>Animals pretreated</td>
<td>6</td>
<td>1.6 ± 0.1</td>
</tr>
<tr>
<td>with aspirin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Iridectomy and</td>
<td>6</td>
<td>1.9 ± 0.3</td>
</tr>
<tr>
<td>pretreatment with aspirin</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Eyes was 35.5 mm Hg 15 min after paracentesis, and the pressure remained elevated for 2 hr. Pressure elevation in dilated eyes peaked at only 27.5 mm Hg (Table II).

Protein. Protein in the secondary aqueous was somewhat higher in iridectomized eyes. Eyes with paracentesis demonstrated an aqueous protein content of 4.03 ± 0.24 gm/100 ml, whereas eyes with sector iridectomy had 4.43 ± 0.12 gm/100 ml. These results indicated an increased vulnerability of the blood-aqueous barrier after sector iridectomy. Slit-lamp examination comparing the two iridectomy groups confirmed the susceptibility of the sector group compared with the group of eyes subjected to peripheral iridectomy. In those eyes iridectomized and with aspirin pretreatment, the secondary aqueous protein content was 1.92 ± 0.29 gm/100 ml (Table III). Protein values similar to those for paracentesis with and without aspirin were obtained previously in our laboratory.\[3 \text{, 7}\] Protein was not measured in the mydriasis group.

Pupil diameter. The pupil diameters in both groups were between 6 and 6.5 mm before paracentesis. There was no change in the first 5 min. Fifteen minutes after paracentesis those animals pretreated with aspirin showed a severe miosis. The aspirin-treated group developed miosis with a pupillary diameter consistently 0.5 to 1.0 mm less than the nonaspirinized group. Similar lack of blockade of miosis by either aspirin or indomethacin was noted in animals whose fifth nerve was stimulated intracranially (Mead and Sears: unpublished observations).

Discussion

It has been shown\[3 \text{, 8}\] that disruption of the blood-aqueous barrier induced by paracentesis is largely reduced by the elimination of endogenous prostaglandin synthesis and release. The increased IOP developed after paracentesis is largely a function of increased inflow of a plasmoid aqueous into the eye through the disrupted barrier.\[9 \text{, 10}\] The current work shows that in addition to contributions made by the disruption of the blood-aqueous barrier and consequent influx of aqueous, pupillary block associated with severe miosis adds to the rise in IOP. When pupillary block is virtually eliminated, as after mydrias or peripheral or complete iridectomy, there is no rise in IOP if animals are also pretreated with aspirin. The pressure-lowering effect of iridectomy alone is about 28%. The effect of aspirin alone is about 57%. (Of course, the effect of aspirin is more variable because of factors such as ocular penetration, absorption, or excretion of the drug.) Allowing for the complexity of the posterior chamber reaction and the variable effect of iridectomy itself on the blood-aqueous barrier, at the very least, a hypothesis can be made concerning additive effect of pupillary block plus prostaglandin synthesis and release to account for the IOP rise after paracentesis. No matter how much prosta-
glandin is synthesized and released to cause hyperemia and breakdown of the blood-aqueous barrier, the consequent increased aqueous influx just simply is not as effective in raising the IOP in animals that have been pretreated by iridectomy to avoid the miotic-induced pupillary block.

Large and small (sector and peripheral iridectomies) gave substantially the same effect. Therefore the surgical effect on the ciliary processes to reduce inflow is probably negligible and can be disregarded. On the other hand, sector iridectomy created an eye more vulnerable to disruption of the blood-aqueous barrier. For this reason, peripheral iridectomy was more effective in reducing the final pressure level, that is, each iridectomy eliminated pupillary block, but more aqueous influx and therefore a higher IOP occurred in the eyes with sector iridectomy. Only a few mydriasis experiments were done because of other possible effects of these drugs on aqueous dynamics. They nevertheless support the main argument. A schema, then, for the ocular hypertensive reaction to paracentesis would appear as follows:

\[
\begin{array}{c}
\text{Pupillary block} \\
\text{Miosis} \rightarrow \text{Increased IOP} \\
\text{Paracentesis} \uparrow \\
\text{Increased aqueous inflow} \\
\text{Hyperemia} \rightarrow \text{Disrupted barrier}
\end{array}
\]

Of additional interest is the fact that pretreatment with aspirin reduced aqueous protein in paracentesis eyes by about 40% (44% in iridectomized eyes), a figure completely in agreement with previous work.\(^3\) Finally, as noted earlier, miosis induced by prostaglandin synthesis and release appears to be aspirin-resistant (refs. 3 and 11 and Mead, Maul and Sears: unpublished observation). We cannot explain why Unger et al.\(^{12}\) were unable to inhibit miosis with indomethacin.

REFERENCES