Anterior Chamber Bleeding After Laser Peripheral Iridotomy

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Importance: To our knowledge, this is the first study to describe the correlation of anterior chamber bleeding after laser peripheral iridotomy (LPI) and antiplatelet therapy.

Objective: To determine the incidence and amount of anterior chamber bleeding after laser peripheral iridotomy in patients whose condition is suggestive of primary angle-closure glaucoma (PACS) who continued their antiplatelet or anticoagulant treatment before undergoing LPI compared with when they discontinued treatment.

Design and Setting: A prospective controlled trial.

Patients: Patients with suspected bilateral primary angle-closure and no other ocular disease who take antiplatelet or anticoagulant medications regularly (from January 2010-October 2011) were enrolled.

Main Outcome and Measure: The incidence of anterior chamber bleeding with and without antiplatelet and anticoagulant therapy.

Results: A total of 104 patients (208 eyes) participated in the study. Thirty-six eyes (34.6%) in the treated and untreated arms bled. The amount of bleeding did not differ significantly when the patient was on or off antiplatelet or anticoagulant treatment, nor did the immediate post-procedure mean intraocular pressure ($P = .13$). The type of antiplatelet or anticoagulant, total laser energy, age, sex, or color of irides were not risk factors for increased bleeding ($P = .156$ for all parameters).

Conclusions: No indication was noted for discontinuing these medications before a high-powered pulsed laser peripheral iridotomy.


Primary angle-closure glaucoma (PACG) accounts for almost half of glaucoma-related blindness worldwide. Laser peripheral iridotomy (LPI) is performed as a prophylactic measure to prevent an acute attack of angle closure and to relieve pupillary block. The procedure results in a substantial widening of the drainage angle in most cases. There is convincing evidence that if primary angle-closure (PAC) is detected early enough, prophylactic LPI probably prevents progression to glaucoma in most cases.

Laser peripheral iridotomies can be performed by either argon or neodymium:yttrium–aluminum–garnet (Nd:Yag) lasers in a continuous, pulsed, or combined mode of application. Reported complications after LPI include iritis, intraocular pressure (IOP) elevations, hemorrhage, ghost images, and posterior synechiae. Anterior chamber bleeding can cause blurred vision for several days after the procedure, elevation of IOP, and macroscopic hyphema with the remote risk factor of endothelial blood staining. It is reasonable to consider that there is a possibility of reducing the incidence and amount of anterior chamber bleeding after LPI by temporarily discontinuing anticoagulant or antiplatelet medications. Whether patients taking antiplatelets or anticoagulants should stop treatment before undergoing an LPI due to concerns about an increased risk for iris bleeding post-LPI has (to our knowledge), however, not been investigated before. The objectives of this study are to evaluate whether discontinuing treatment by antiplatelets or anticoagulants influences the amount of LPI-associated anterior chamber bleeding and to identify risk factors for its occurrence following this procedure.

Methods

This was a prospective controlled trial with a split body design. Ethical approval was ob-
tained from the Ethical Review Board of Tel Aviv Sourasky Medical Center. The study was conducted in the Department of Ophthalmology between January 2010 and October 2011 in accord with the tenets of the World Medical Association’s Declaration of Helsinki. All the study participants were being treated with anticoagulants, for example, warfarin sodium (Coumadin; Bristol Meyers Squibb), or antiplatelets, for example, aspirin and clopidogrel bisulfate (Plavix; sanofi aventis US) therapy for various reasons and for various periods. Inclusion criteria were (1) the use of antiplatelet and anticoagulant medication; (2) primary angle-closure suspects (PACS) in both eyes as defined by static and dynamic gonioscopy, as detailed later; (3) no other ocular disease that precluded an examination of the angle; and (4) a primary physician approval of a 2-week discontinuation of medications.

Exclusion criteria were any corneal disease that precluded an examination of the angle, a cLobsable angle but secondary to other ocular diseases, for example, uveitis, and glaucoma that was being treated with antiglaucoma medication.

Gonioscopiny was performed with a 4-mirror Goldmann goniolens or a 4-mirror Zeiss lens. PACS patients were identified as having 6 or more clock hours of angle circumference in which the posterior (usually pigmented) trabecular meshwork was not visible. A dynamic examination was performed after increasing the length and width of the beam and increasing the brightness. The participant was asked to look toward the mirror of the gonioscope, bringing the adjacent rim of the gonioscope over the central cornea. Pressure was exerted on the rim of the gonioscope to indent the central cornea. If iridotrabecular contact was not reversed satisfactorily, a dynamic examination with a 4-mirror gonioscope (Ocular Sussman 4-Mirror Gonioscope; Ocular Instruments) was carried out to determine if peripheral anterior synechiae were present, defined as acquired adhesions of the iris to the corneoscleral wall crossing the scleral spur for a width of 1 clock-hour or more and resulting in tenting of the peripheral iris. The angle configuration was graded in all 4 quadrants according to the Shaffer grading system and also was recorded as the circumference in which the pigmented trabecular meshwork was not visible.

The right eye of each patient was selected to undergo the procedure while the patient continued to take antiplatelet or anticoagulant medications. The fellow left eye underwent LPI 2 weeks after discontinuing the medication.

Written informed consent was obtained after the potential adverse effects and benefits of LPI were explained in detail to each patient. Laser peripheral iridotomy was performed by a single surgeon (S.K.) using an Nd:Yag laser (Visulas YAG III; Carl Zeiss Meditec). One drop of pilocarpine, 2%, was instilled before the procedure and examined in the clinic 4 days later. There was no need for re-treatment or treatment at an alternative site. The IOP was measured before and 1 hour after the procedure.

### Statistical Analysis

Baseline IOPs were compared between the right and left eyes using the paired t test for continuous variables. The McNemar-Bowker statistical tests were used to compare iris bleeding between the 2 eyes; with regard to the specific anticoagulant or platelet medication and the color of the irides, the t test was used to compare mean age and total laser energy between anterior chamber bledders and nonbledders.

The color of the irides and the patient’s sex were compared between bledders and nonbledders using the χ2 test. Association between right eye and left eye bleeding was tested using the Fisher exact test.

### Results

The study included 104 subjects diagnosed as having bilateral PACS. There were 68 women (65.4%); the mean (SD) age of the cohort was 69.1 (11.0) years (age range, 42-88 years). The anticoagulants most commonly used were aspirin (51 patients [49.0%]), warfarin (34 patients [33.0%]), and clopidogrel (19 patients [18.0%]). There was no statistically significant (P = .06) difference in IOP between the pre-LPI and post-LPI measurements with or without anticoagulant therapy (a difference [SD] in IOP of 2.4 ± 5.0 mm Hg OD and 0.3 ± 2.4 mm Hg OS).

The incidence of anterior chamber bleeding was comparable with and without anticoagulant therapy (34.6%). The amount of bleeding, graded as 0 through 3, was compared between the right and left eyes. The number of patients without any bleeding (grade 0) was similar in both groups (Table 1). Minor bleeding (grade +1) was recorded in 29.8% of the right eyes and 33.7% of the left eyes (P = .14). Grade 2 bleeding was recorded in 4.8% of the right eyes and 1.0% of the left eyes (P = .14). No eye had grade 3 bleeding in this study. There was no statistical difference in the amount of anterior chamber bleeding with respect to the various anticoagulant or antiplatelet therapies that were used. Sixteen patients (31.4%) who were taking aspirin had anterior chamber bleeding grades 1 and 2 in the right eye compared with 20 patients (39.2%) taking aspirin who had anterior chamber bleeding.
bleeding grades 1 and 2 in the left eye (P = .42, Table 2). Warfarin was associated with bleeding in the right eye in 14 patients (41.2%) and in the left eye in 12 patients (35.3%) (P = .75). Clopidogrel was associated with bleeding in the right eye in 6 patients (31.6%) and in the left eye in 3 patients (15.8%) (P = .25). Darker-colored irides were slightly less associated with a tendency for anterior chamber bleeding than lighter irides (blue-green), but the difference was not significant (P = .07).

The total laser energy used to create a patent iridotomy was not associated with the occurrence of anterior chamber bleeding (P = .25). Older age was slightly associated with more anterior chamber bleeding, irrespective of whether the patient continued to use antiplatelets or anticoagulants, but the difference was not statistically significant (P = .06). The only correlation found to be statistically significant was between the color of the irides and the total laser energy used to create a patent LPI (P = .004).

When we compared the association between right and left eye bleederers, we found that 61.1% of the patients who bled in the right eye also bled in the left eye and that 79.4% of the patients who did not bleed in the right eye also did not bleed in the left eye. This correlation was found to be statistically significant (P < .001).

<table>
<thead>
<tr>
<th>Anticoagulant</th>
<th>No. of Patients</th>
<th>No. of Eyes, Right/Left</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin</td>
<td>51</td>
<td>16/20</td>
<td>.42</td>
</tr>
<tr>
<td>Warfarin sodium</td>
<td>34</td>
<td>14/12</td>
<td>.75</td>
</tr>
<tr>
<td>Clopidogrel bisulfate</td>
<td>19</td>
<td>6/3</td>
<td>.25</td>
</tr>
</tbody>
</table>

Many patients who are candidates for LPI take antiplatelets and anticoagulants for a variety of reasons. To our knowledge, no study has previously reported whether such medications should be discontinued before the patient undergoes the procedure with a high-power pulsed laser in terms of an associated LPI-related risk of anterior chamber bleeding.

We found no difference in the incidence and amount of bleeding in patients undergoing LPI with and without antiplatelet or anticoagulant treatment, irrespective of the medication. We also analyzed the risk factors for bleeding after pulsed LPI, given that laser iridotomies are associated with a number of adverse effects, most common of which are iritis, IOP elevations, and anterior chamber bleeding. Indeed, anterior chamber bleeding immediately after Nd:YAG laser iridotomies was reported to occur in up to 40% of patients.

Iridotomies by pulsed Nd:YAG lasers use plasma formation and consequent photodisruption instead of coagulation of proteins created by continuous-wave lasers, such as argon, diode, and frequency-doubled YAG machines. The use of Nd:YAG lasers results in relatively more bleeding and pigment dispersion. Moreover, the deposition of debris from blood and pigment in the juxtaocular trabecular meshwork may impede aqueous outflow and cause IOP elevation.

In a recent study by Jiang et al, the amount of anterior chamber bleeding following Nd:YAG laser iridotomy was 30.7%, and 40.2% of eyes experienced IOP spikes following the procedure. To avoid anterior chamber bleeding after LPI, some authors suggest pretreatment thinning with a few continuous-wave laser spots to seal local vessels and solve the bleeding problem.

The risk factors for the development of iris bleeding in connection with LPI have never been studied. We selected several parameters that were likely to increase the risk of bleeding. One was the patient’s age: there was only a slight tendency toward more bleeding among older patients. This tendency was also observed in many other articles in terms of an increased propensity toward gastrointestinal tract and vaginal bleeding in the elderly population, suggesting that advanced age is an independent risk factor for hemorrhagic complications. Another was the color of the irides and the total laser energy: there was a tendency toward more bleeding in lighter-colored irides than darker-colored ones (P = .07). The total energy used to create a patent iridotomy was not correlated with the amount of iris bleeding (P = .25) but was significantly correlated with the color of the irides (P = .004). Notably, pure YAG laser iridotomy often requires high levels of energy to achieve a patent iridotomy in dark irides, a difference in color that had been reported by several other investigators.

Aspirin and clopidogrel are among the most extensively studied antiplatelet agents to date. They are inevitably associated with a risk of hemorrhage because the same pathways by which antiplatelet drugs antagonize platelet activation or aggregation increase the risk of bleeding. Most spontaneous bleeding in patients who are being treated with antiplatelet drugs occurs in the gastrointestinal tract, with an incidence of 2% to 3% with dual antiplatelet therapy. Bleeding is also common at puncture and surgical sites, with an incidence of about 1% to 2%.

Warfarin is an antithrombotic medication whose primary mechanism of action is antagonism of vitamin K procoagulant factors. Estimates of bleeding rates for warfarin vary widely depending on the study design: the annual incidences reported by Landefeld and Beyth were 0.6% for fatal bleeding, 3.0% for major bleeding, and 9.6% for major or minor bleeding events.

Standard practice has been to stop aspirin therapy 7 to 10 days before elective surgery for fear of excessive bleeding. Clopidogrel and warfarin therapies are usually stopping 5 days before elective surgery. In this study, we stopped medications for 2 weeks with the approval of the primary physician.

The limitations of the current study were that the eye which underwent LPI with or without systemic treatment was not randomized. The arbitrary selection of right eyes to LPI with antiplatelet or anticoagulant treatment and left eyes without treatment may bias the results. The LPI was conducted by a single operator (S.K.) who was unmasked to the study design. Another limitation is that...
the grouping according to medication is not entirely homogeneous, with 70 patients receiving antiplatelet therapy (aspirin and clopidogrel) and 34 receiving anticoagulant therapy (warfarin). Neither the target nor the international normalization ratio during LPI was recorded in the warfarin-treated group, a factor that can bias the results. We found that bleeding in one eye was associated with an increased risk of bleeding in the other, suggesting that specific patients may have a greater tendency toward bleeding, irrespective of the medications taken.

In conclusion, to our knowledge, this is the first article about the percent and degree of anterior chamber bleeding immediately after LPI in patients taking antiplatelet or anticoagulant medications. We concluded that the continued use of antiplatelets or anticoagulants was not associated with significantly increased anterior chamber bleeding following LPI. We believe that treatment with these agents should not be discontinued prior to performing an LPI with a high-power pulsed laser.

Submitted for Publication: May 7, 2012; final revision received September 21, 2012; accepted October 2, 2012. Published Online: March 28, 2013. doi:10.1001/jamaopthalmol.2013.1642

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Conflict of Interest Disclosures: None reported.

REFERENCES