Large–Spot Size Transpupillary Thermotherapy for the Treatment of Occult Choroidal Neovascularization Associated With Age-Related Macular Degeneration

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Objective: To describe the outcome of patients with occult choroidal neovascularization in age-related macular degeneration treated with transpupillary thermotherapy.

Design: Prospective, nonrandomized, nonmasked case series.

Methods: All patients with age-related macular degeneration with a predominantly occult choroidal neovascular membrane and an initial visual acuity of 20/400 or better were offered treatment using transpupillary thermotherapy. The treatment consisted of using a diode laser, a spot size of about 3000 to 6000 µm delivered over 60 seconds, and a power of 600 to 1000 mW.

Main Outcome Measures: A stable, improved, or worsened visual acuity and the need for additional treatment.

Results: Sixty-nine patients were treated. All patients have been followed up for at least 6 months. At the 6-, 9-, and 12-month follow-up visits, 71% of patients have stable or improved visual acuity and 29% have lost 2 or more lines of visual acuity on the Snellen letter chart.

Conclusion: Large–spot size transpupillary thermotherapy is effective in stabilizing the visual acuity in those patients who have occult choroidal neovascularization due to age-related macular degeneration.

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A GE-RELATED MACULAR degeneration (AMD) is one of the leading causes of blindness in the Western world. The most common cause of visual loss is the formation of choroidal neovascularization (CNV).1 Compared with the natural history, thermal laser treatment is more effective in preventing significant loss of visual acuity in patients with extrafoveal and juxtafoveal CNV.2,3 In patients with neovascularization under the fovea, the prognosis is much more guarded. Thermal lasers have been the mainstay of treatment for subretinal neovascular membranes. Unfortunately, thermal lasers cause damage to the neurosensory retina resulting in a permanent scotoma. For those patients with subfoveal neovascularization, the Macular Photocoagulation Study Group4 showed a small benefit by treating these lesions with a thermal laser.

The diode laser has a theoretical advantage over other wavelengths of light because there is little absorption in the xanthophyll layer and, thus, damage to the nerve fiber layer is minimized. Additionally, compared with the argon laser, the diode laser is poorly absorbed by hemoglobin5 allowing an improved ability to treat through preretinal and subretinal hemorrhage. The wavelength of the diode laser (810 nm) is mainly absorbed by melanin at the level of the retinal pigment epithelium and choroid, enabling treatment of choroidal lesions.7 Long-duration, low-irradiance diode laser has been used to treat choroidal melanomas8,9 and, in preliminary trials, to treat CNV (transpupillary thermotherapy [TTT]).10,11 The recent reports on the use of TTT for subfoveal CNV show some success in the treatment of both classic and occult CNV. Because occult neovascular membranes are often difficult to precisely define and may originate from more than one foci, we used a large–spot size diode laser to ensure that the treatment area would cover large, multifocal or diffuse occult CNV. We investigated the use of large-spot size TTT for occult CNV in patients who had AMD.

METHODS

All patients in this study were initially treated between October 1, 2000, and De-
paracaine hydrochloride was applied to the eye prior to the 3000 µm. The spot size was set at 3000 µm. Topical 0.5% presence of AMD.

At the initial visit and all subsequent visits the patient had a Snellen visual acuity measured and underwent a general ophthalmologic examination, to include biomicroscopic examination of the macula. Fluorescein angiography was performed at the initial visit and at each subsequent 3-month visit. The patients were informed of the results of preliminary trials that had been published and given the option of observation vs treatment.

Transpupillary thermotherapy (TTT) was delivered via a slitlamp using an infrared diode laser at 810 nm. The spot size was set at 3000 µm. Topical 0.5% proparacaine hydrochloride was applied to the eye prior to placement of an area centralis lens (magnification of laser spot, ×0.94) or a quadrascpheric lens (×1.97 magnification of laser spot, resulting in a spot size of 5910 µm) (Volk Optical Inc., Mentor, Ohio). Continued observation through the lens ensured proper fixation. The treatment consisted of a single spot with a duration of 60 seconds. The power used ranged from 600 to 1000 mW. The power was begun at 750 mW for the area centralis lens and at 1000 mW for the quadrascpheric lens and was adjusted downward if there was any retinal whitening noted, if the patient experienced any pain or a burning sensation, or if the patient or physician heard a popping sound.

The patient was seen 6 weeks after treatment and 3 months after treatment, then every 3 months thereafter. Retreatment was performed at 3-month intervals if there was persistent leakage noted in the late stages of the fluorescein angiogram. The average visual acuity was obtained by calculating the logarithm of the minimal angle of resolution (ie, Snellen visual acuity), taking the mean of these figures, and converting the antilog of the mean to a Snellen visual acuity.

Sixty-nine patients (18 men [26%] and 51 women [74%]) elected to undergo treatment with TTT. The average age was 78 years (age range, 66-91 years). Review of the fluorescein angiogram showed that all 69 lesions were predominantly occult. Two patients developed a retinal pigment epithelial tear after TTT, but no other complications were noted. The laser spot size was about 6000 µm in 65 patients (94%) and about 3000 µm in 4 patients (6%).

Table 1 gives the duration of follow-up visits and the retreatment of the original 69 patients. All patients had at least 6 months of follow-up (some patients returned for a 9- or 12-month follow-up visit but had not returned for the 6-month follow-up visit). Each patient had an average of 1.93 treatment sessions in the first year (range, 1-3 treatment sessions). Twenty-one patients (30.4%) had 1 treatment, 32 patients (46.4%) had 2 treatments, and 16 patients (23.2%) had 3 treatments (Table 1).

The mean visual acuity at the initial visit was 20/177, at the 3-month visit it was 20/208, at the 6-month visit it was 20/230, at the 9-month visit it was 20/208, and at the 12-month visit it was 20/229. The visual acuity at each of the follow-up visits was compared with the initial visual acuity. Stable or improved visual acuity was defined as a loss of 2 or more lines of visual acuity on the Snellen letter chart on the fluorescein angiogram. The average visual acuity on the Snellen letter chart.

Table 1. Follow-up and Retreatment of the Original 69 Patients*†

<table>
<thead>
<tr>
<th>Follow-up Visit, mo</th>
<th>Treated</th>
<th>Retreatment†</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>69 (100)</td>
<td>31 (45)</td>
</tr>
<tr>
<td>6</td>
<td>65 (94)</td>
<td>18 (28)</td>
</tr>
<tr>
<td>9</td>
<td>51 (74)</td>
<td>10 (20)</td>
</tr>
<tr>
<td>12</td>
<td>28 (41)</td>
<td>5 (18)</td>
</tr>
</tbody>
</table>

*Data are given as the number (percentage) of patients.
†Twenty-one patients had 1 treatment, 32 patients had 2 treatments, and 16 patients had 3 treatments during the follow-up period.

Table 2. Visual Acuity

<table>
<thead>
<tr>
<th>Visit, mo</th>
<th>No. (%) of Patients</th>
<th>Mean Visual Acuity</th>
<th>Patients With Stable or Improved Visual Acuity*</th>
<th>Patients With Worsened Visual Acuity*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial</td>
<td>69</td>
<td>20/177</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>69 (100)</td>
<td>20/208</td>
<td>56 (81)</td>
<td>13 (19)</td>
</tr>
<tr>
<td>6</td>
<td>65 (94)</td>
<td>20/230</td>
<td>46 (71)</td>
<td>19 (29)</td>
</tr>
<tr>
<td>9</td>
<td>51 (74)</td>
<td>20/208</td>
<td>36 (71)</td>
<td>15 (29)</td>
</tr>
<tr>
<td>12</td>
<td>28 (41)</td>
<td>20/229</td>
<td>20 (71)</td>
<td>8 (29)</td>
</tr>
</tbody>
</table>

*Data are given as number (percentage) of patients.

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ing the tissue temperatures as much as over 40°C. Photodynamic therapy, on the other hand, creates a photochemical reaction in which a long-pulse, very low-irradiance laser activates a chemical photosensitizer that has been absorbed in the target tissue causing damage to and closure of the CNV. Transpupillary thermotherapy uses a long pulse and large spot size to induce hyperthermia and apoptosis. Transpupillary thermotherapy raises tissue temperatures about 10°C. For very long exposures, heat convection, because of choroidal blood flow, moderates the chorioretinal temperature rise.

When used in patients who have AMD, it delivers the light at a threshold or subthreshold level with a barely visible or an invisible lesion in the retina and choroid. It is thought that raising the temperature 5°C will cause heat shock, protein denaturation, and cell death. Melanin in the retinal pigment epithelium and choroid is the primary light absorber in retinal photocoagulation. These factors should help to limit the damage to the neurosensory retina. A histopathologic study done on TTT-treated eyes with a choroidal melanoma showed thrombosis of the tumor vessels.

Fluorescein angiography shows hypofluorescence and diminished leakage at 1 and, to a lesser extent, 4 weeks after TTT. This closure of the choroidal vasculature may be caused by endothelial damage due to hyperthermia at the target tissue.

The results from our study show that visual acuity is stabilized in 71% of patients at the 6-, 9- and 12-month follow-up visits (Table 2). Although statistically there was not a significant improvement in visual acuity, neither was there a significant decrease in visual acuity. This compares favorably with the results of other studies on TTT in which 63% to 86% were stable, with variable follow-up, and with the natural history of occult CNV in which only 38% of patients were stable after 9 to 12 months. Photodynamic therapy for purely occult CNV did not seem to fare any better than the natural history studies. In patients treated with photodynamic therapy for occult CNV, only 34% of those treated had stable or improved visual acuity at 12 months. In the control group, 23% of those treated had stable or improved visual acuity. Comparing the results of these studies has its limitations as each study had its own inclusion and exclusion criteria, vastly different forms of treatment, variable methods of measuring visual acuity, and different follow-up periods.

The ideal laser settings for TTT have not been determined. The previous studies using TTT for CNV in AMD have used different settings. The spot size varied from 800 to 3000 μm. The power used was 300 to 1000 mW, and the number of spots varied from 1 to an average of 4.25 per treatment session. The goal in all of the studies is to have minimal or no retinal whitening. In our study we used a large spot size of about 6000 μm in most of our patients. The large spot size was used to cover a broad area as the full extent of an occult CNV may not be able to be determined on fluorescein angiography alone. Often an occult CNV will have several points of origin. The patients in our study were treated with 600 to 1000 mW of power. None of the patients developed any clinical evidence of retinal whitening, but the power was adjusted downward only when the patient felt pain or a burning sensation or when the physician or patient heard an audible pop. The audible pop or retinal whitening indicates a suprathreshold treatment level. Of the 133 treatment sessions completed, the power was lowered for 12 patients (9%) because of pain or a burning sensation or an audible pop.

We had 2 patients (3%) who developed a tear in the retinal pigment epithelium after TTT. Thompson has also reported a tear in the retinal pigment epithelium after TTT. Others have reported a complication rate as low as a 0% and as high as 9%. Other complications noted to occur after TTT for a choroidal melanoma include vascular occlusion, macular edema, retinal neovascularization, and optic nerve edema. The increased risk of TTT complications in patients with a choroidal melanoma may be due to the higher-power settings used for these patients.

The use of large-spot size TTT seems to be an effective treatment of occult CNV membranes in AMD. Our results are comparable to the results of other studies using smaller spot sizes. When compared with photodynamic therapy for predominantly occult CNV, TTT seems to have a better success at stabilizing visual acuity, although there have not been any controlled studies with TTT. Other than the results of apparent improved visual acuity, TTT does not require the time and cost of photodynamic therapy and because no medication is needed, there are fewer adverse effects from TTT.

Although our study was prospective, we did not use standardized visual acuity charts (eg, Early Treatment Diabetic Retinopathy Study chart) and we used only historical controls. These factors may have induced bias in our analysis. The exact role of TTT in patients with subfoveal CNV in AMD and the laser treatment variables will only be answered after a large randomized, prospective, multicenter treatment trial is conducted.

Table 3. Comparison of Visual Acuity Results to Other Treatment Trials

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients With a Stable or Improved Visual Acuity</th>
<th>Patients With a Loss of 2 or More Lines of Visual Acuity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Predominantly or entirely occult</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TTT (this study, 3 mo)</td>
<td>81</td>
<td>19</td>
</tr>
<tr>
<td>TTT (this study 6, 9, and 12 mo)</td>
<td>71</td>
<td>29</td>
</tr>
<tr>
<td>TTT (other studies, variable follow-up)</td>
<td>63-86</td>
<td>14-37</td>
</tr>
<tr>
<td>Natural history (9-12 mo)25</td>
<td>38</td>
<td>62</td>
</tr>
<tr>
<td>PDT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Occult (12 mo)15</td>
<td>34</td>
<td>66</td>
</tr>
<tr>
<td>Occult control (12 mo)15</td>
<td>23</td>
<td>77</td>
</tr>
<tr>
<td>Predominantly classic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PDT (12 mo)15</td>
<td>38</td>
<td>62</td>
</tr>
<tr>
<td>PDT control (12 mo)13</td>
<td>24</td>
<td>76</td>
</tr>
</tbody>
</table>

Abbreviations: PDT, photodynamic therapy; TTT, transpupillary thermotherapy.

*Data are given as percentages of patients.
†Visual acuity at each follow-up visit is compared with the initial visual acuity.
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REFERENCES