# Long-term efficacy of transpupillary thermotherapy for subfoveal choroidal neovascularization in age – related macular degeneration

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#### Abstract

•AIM: To determine the long-term efficacy of transpupillary thermotherapy (TTT) in the treatment of subfoveal choroidal neovascularization (CNV) in age-related macular degeneration (AMD).

• METHODS: Fourteen eyes of 14 patients with subfoveal CNV secondary to AMD were treated with diode laser (810nm) TTT. The mean age was 67.1 years. Complete ophthalmic examination was done, color fundus photographs and macular optical coherence tomography scans were taken, fluorescein and indocyanine green angiography were performed during initial and at subsequent follow-up examinations. Treatment was given in one minute using 2-3mm spot sizes, and laser power settings were between 650-800mW. The follow-up period was between 5 and 64 months and the mean was 28.6 months.

• RESULTS: There was subfoveal classic CNV in 10, predominantly classic CNV in 2, minimally classic CNV in 1, and type 1 occult CNV in one of the fourteen eyes. Four patients were noted to have post-treatment hemorrhage which was absorbed in a short time. Macular non-perfusion occurred in one patient immediately after treatment. Most of the eyes demonstrated a decrease in exudation during the follow-up. With a mean follow-up of 28.6 months, visual acuity improved in 5, remained the same in 8 and decreased in 1 of the 14 eyes.

•CONCLUSION: Transpupillary thermotherapy is shown to close subfoveal CNV with rapid resolution of subretinal fluid while maintaining visual function in patients with AMD. It may be performed as an alternative laser treatment in classic and predominantly classic subfoveal choroidal neovascularization due to AMD. • KEYWORDS: transpupillary thermotherapy; CNV; subfoveal CNV; age-related macular degeneration

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#### INTRODUCTION

C horoidal neovascularization (CNV) is the major cause of severe visual loss in age-related macular degeneration (AMD). Laser photocoagulation treatment can reduce the incidence of visual loss in cases of extrafoveal and juxtafoveal CNV<sup>[1,2]</sup>. The Macular Photocoagulation Study Group showed that most patients with juxtafoveal CNV experienced recurrence and patients with subfoveal membranes experienced rapid visual loss following treatment <sup>[3,4]</sup>. These findings led the investigators to develop new treatments for subfoveal CNV.

Transpupillary thermotherapy (TTT) has emerged from tumor treatment and has recently been adopted for CNV in AMD<sup>[5]</sup>. Reichel *et al*<sup>[6]</sup>, first reported the use of TTT for the treatment of occult subfoveal choroidal neovascularization secondary to age-related macular degeneration. In their pilot study, Reichel and colleagues found that vision improved in 19% of patients and stabilized in 56%, with a decrease in exudation in 94%. Optical coherence tomography demonstrated vascular membrane resolution with a restoration of the macular anatomy. Additional studies have shown similar rates of success in the treatment of occult CNV <sup>[7-9]</sup>. Favorable results of TTT were also achieved in a small series of predominantly classic CNV<sup>[10]</sup>.

Here we report 28.6-month results of a series of patients with subfoveal CNV secondary to AMD treated with TTT.

<sup>·</sup>Clinical Research·

#### MATERIALS AND METHODS

We conducted a retrospective review of patients with classic or predominantly classic subfoveal CNV treated with transpupillary thermotherapy. All patients had pre-treatment Snellen visual acuity, slit-lamp microscopy, funduscopy, color fundus photography, fluorescein angiography (FA) and optical coherence tomography (OCT) of the macular area. Indocyanine green angiography (ICGA) was performed in selected cases.

Treatment was delivered using an infrared diode laser at a wavelength of 810nm equipped with a modified slit-lamp adapter with an adjustable beam width (Iris Medical Instruments, Mountain View, CA). After FA was performed the lesion size was measured to determine the appropriate laser spot size setting. For a 3mm spot size, a maximum of 800mW (range 650-800mW) was delivered to the retina for a total of 60 seconds with continuous observation through the slit-lamp. A three-mirror Goldmann lens was used. For smaller spot sizes, the power decreased proportionally. If the lesion size was greater than 3mm, overlapping treatments were applied. The end-point for treatment was an area of no visible color change throughout the course of treatment. If retinal whitening was observed during treatment, the power was adjusted by a decrease of 10% and the treatment was re-started.

Retreatment was instituted when fluorescein leakage had not regressed or had increased after the first TTT concomitantly with a significant decline of visual acuity.

#### RESULTS

Fourteen eyes of 14 AMD patients were included in the study. There were 7 men and 7 women, with a mean age of 67.1 years (range 52-78 years). All patients had symptoms, such as metamorphopsia or significant visual acuity loss due to subfoveal choroidal neovascularization. Ten patients had classic, 2 had predominantly classic, one had minimally classic, one had occult type 1 (fibrovascular pigment epithelial detachment) CNV. The mean follow-up period was 28.6 months (range 5-64 months).

Ten eyes (72%) received one application of TTT, 3 eyes (21%) two applications and one eye (7%) three applications. Retreatment was needed in 2/14 eyes (14%) at 2 months, in 1/14 eye (7%) at 7 months, in 1/14 eye (7%) at 9 months. The mean interval before retreatment with TTT was five months and the mean number of treatments in fourteen eyes was 1.4.



Figure 1 Macular non-perfusion immediately after TTT



Figure 2 A:Fluorescein angiography shows minimally classic CNV; B:Three years after TTT, the same eye

Four eyes (28%) were noted to have posttreatment hemo-rrhage which was absorbed in a short time. One eye (7%) suffered from a macular non-perfusion with an acute decline in vision after TTT (Figure 1). At the end of a 49-month follow-up, visual acuity was measured by counting fingers at two meters.

At the 28.6-month follow-up, visual acuity had improved in five eyes (36%) and deteriorated in 1 eye (7%). Thus, 13 of 14 eyes (93%) remained stable or improved in vision. Deterioration of visual acuity was due to postoperative macular non-perfusion in one eye.

With OCT, the fundi were scanned on the horizontal and

vertical planes through choroidal neovascularization. Subfoveal CNV was identified as a highly or moderately reflective mass that protruded through the retinal pigment epithelium (RPE). In one case of fibrovascular pigment epithelial detachment, OCT showed an elevation of the RPE above a backscattering area corresponding to fibrovascular proliferation. CNV was usually accompanied by subretinal fluid, retinal edema, intraretinal cysts that appeared as non-homogenous hyporeflective areas.

One month after TTT and during the follow-up, OCT showed decreased subretinal and intraretinal fluid and diminished retinal elevation in 93% of the eyes. Late staining of subretinal fibrosis was observed in all cases on fluorescein angiography (Figure 2).

#### DISCUSSION

Transpupillary thermotherapy for age-related macular degeneration was introduced by Reichel et al [6]. Since that time, several laser surgeons have also investigated its utility in the treatment of primarily occult choroidal neovascularization <sup>[11-14]</sup>. While none of these studies was a randomized controlled trial, the general results of these studies indicate that TTT treatment appears to be associated with the stabilization of visual acuity at six to nine months in about 2/3 to 3/4 of the cases with reduction of subretinal fluid. A pilot study by Reichel and colleagues using TTT for occult CNV has shown stabilization of vision in this group <sup>[6]</sup>. Sixteen eyes of 15 patients with occult CNV were treated with TTT and followed for 6 to 25 months. This study showed that vision improved or stabilized in 75% of eyes and subretinal fluid decreased in 94% of eyes. Another study by Newsom and colleagues studied the effect of TTT on 32 eyes with occult CNV followed for a mean of 7.2 months<sup>[10]</sup>. Stabilization or improvement of vision was obtained in 72% and reduction of exudation in 78% of the eyes. Kim and colleagues <sup>[12]</sup> evaluated the efficacy of TTT in 48 eyes with occult CNV. Visual acuity was stable or improved in 62.5% and subretinal fluid reduced in 61% of the eyes in their study. The prospective study on predominantly occult subfoveal CNV done by Algvere and colleagues<sup>[15]</sup> indicated that visual acuity could be stabilized or improved by TTT in 74% of patients at 6-month follow-up. The results of our study on classic and predominantly classic CNV indicate that TTT effectively stabilizes CNV process in the long term. The majority of the patients treated with TTT maintained or gained visual acuity (93%).

Patients with classic CNV in our trial had average 1.4 treatments in 28.6 months compared with 2.3 treatments in 28 months for 10 patients with classic CNV in Newsom and colleagues' study <sup>[16]</sup>. Twenty-eight patients with occult, classic and mixed CNV in Agarwal *et al*'s study, had an average of 1.86 treatments in 15.3 months <sup>[17]</sup>.

Several complications have been reported following TTT for uveal tumors, including branch retinal vein and artery occlusions and retinal and choroidal hemorrhage. However, low power settings used in TTT for CNV have meant that complications are rare and patient tolerance is good. TTT treatment has been well tolerated in the initial series of reports <sup>[4-6]</sup>. One eye in our study had a unique complication of macular non-perfusion immediately after treatment. The patient noted an immediate drop in vision with the clinical findings of retinal whitening and attenuation of the perifoveal retinal arteriols. A similar complication was observed in one of the 81 eyes treated with TTT in Ahuja et al's study [11]. Their patient had pre-existing areas of geographic RPE atrophy in the macular region adjacent to the zone of treatment, which could have diminished the heat sink role of the choroid and potentiated the hyperthermic effect. We did not observe a similar finding in our patient.

In this study the 28-month results for patients treated with TTT for classic and predominantly classic CNV show good visual stability with little visual loss and few complications.

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