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Medical Policy Manual

Topic: Transpupillary Thermotherapy for Treatment of Choroidal Neovascularization

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Section: Surgery

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IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Transpupillary thermotherapy (TTT) is a technique in which heat is delivered through the pupil using a modified diode laser to treat choroidal neovascularization (CNV), a common cause of adult-onset blindness. TTT uses a lower power laser for more prolonged periods of time and is designed to gently heat subfoveal choroidal lesions while limiting damage to the overlying retinal pigment epithelium.

CNV is most commonly associated with age-related macular degeneration (AMD). While laser photocoagulation has been used to treat CNV, patients with subfoveal lesions are generally not candidates for this treatment due to the risk of an immediate reduction in central vision, outweighing any treatment advantage. Photodynamic therapy (PDT) has been used with success in treating subfoveal CNV; the treatment has shown the greatest success in treating patients with classic CNV (as opposed to occult CNV), as defined angiographically. There is ongoing research interest in the use of TTT to treat subfoveal CNV with an "occult" angiographic pattern.

In addition, CNV can occur as a secondary symptom to central serous chorioretinopathy (CSC). In about 90% of cases, CSC resolves spontaneously with detachment resolution within 3 months. Recurring or chronic CSC can be treated with focal laser photocoagulation if the leaks are extrafoveal. Although laser treatment may shorten the duration of symptoms, it does not have any impact on the final vision or the recurrence rate of CSC. In addition, laser photocoagulation causes collateral damage creating symptomatic scotomas and a risk of triggering secondary CNV. Photodynamic therapy is not a

standard treatment for CSC due to complications that may include CNV, although low-fluence PDT is being evaluated.

MEDICAL POLICY CRITERIA

Transpupillary thermotherapy is considered **investigational** as a treatment of choroidal neovascularization secondary to ocular conditions, including but not limited to age-related macular degeneration.

SCIENTIFIC EVIDENCE

In order to determine the safety and effectiveness of transpupillary thermotherapy (TTT) for treatment of choroidal neovascularization (CNV), large, well-designed randomized controlled trials that compare this therapy to standard medical treatment (photodynamic therapy) are needed.

Literature Appraisal

There are minimal published data regarding TTT, consisting mostly of a few small randomized trials and several case series.

Randomized Controlled Trials (RCTs)

- A 2008 RCT with 98 patients reported similar outcomes between transpupillary thermotherapy (TTT) (136 mW/mm) and photodynamic therapy (PDT).[1] Patients with occult choroidal neovascularization (CNV) were randomized to either TTT with sham PDT (n=52), or to PDT with sham TTT (n=46); retreatment was given if leakage was documented by fluorescein angiography (follow-up of 6, 12, 18, 24, 36, and 48 weeks). With a mean of 3.0 treatments in the TTT group and 2.3 treatments in the PDT group, a similar percentage of patients had lost fewer than 15 letters at 12 months (75% for TTT and 74% for PDT). Differences in the proportion of patients to have preserved or improved best corrected visual acuity were not significant comparing the TTT group (37%) with the PDT group (24%); neither were decreases in foveal thickness significant (15% vs. 24%, respectively). Patient-reported visual function from this trial was reported in 2010.[2] Outcomes on the National Eye Institute Visual Function Questionnaire 25 were similar in patients treated with TTT (change of +1.2) or PDT (change of +0.7) at 12 months, but the study was underpowered to detect differences in this outcome measure. Overall, no treatment benefit was associated with TTT over PDT in this small group of patients.

- In 2012, Nowak et al. reported on 222 eyes with age-related macular degeneration (AMD) treated with TTT, 100 eyes treated with PDT and 104 eyes treated with intravitreal bevacizumab.[3] Assignment into the 3 groups was based on the angiographic appearance of CNV, and patients who did not meet criteria for the randomized comparison of bevacizumab and PDT were treated with TTT. Following treatment with TTT, there was a mean decline of visual acuity 0.05 logarithm of the minimum angle of resolution (log MAR), compared to a decline of 0.12 log MAR following PDT and improvement of 0.03 log MAR following treatment with intravitreal bevacizumab. Out of the 222 eyes treated with TTT, visual acuity improved in 14.9%, remained unchanged in 64.4%, and was reduced in 20.7%. This study is limited by selection bias, lack of long-term follow-up, and differences in baseline visual acuity in the 3 groups.

- In 2012, Soderberg et al. randomized 100 patients with neovascular age-related macular degeneration (AMD) to low-dose TTT and intravitreal ranizumab or to sham TTT and intravitreal ranizumab.[4] At 24-month follow-up (78 patients), quarterly TTT was found to decrease the mean number of ranibizumab injections from 8.0 to 6.3 with no significant difference between the sham and active TTT groups in BCVA (+4.0 vs. +0.9, respectively). Thus, 7 quarterly treatments with TTT resulted in a mean reduction of 1.7 ranibizumab injections. It was unclear whether investigators were blinded when assigning patients to either treatment group. A blinded evaluation found no significant difference between the sham and active TTT groups in central retinal thickness (-49.9% vs. -36.4%) or lesion area (-0.3% vs. -10.6%, both respectively).

- Two small randomized trials (n=28 and 25) reported no benefit of TTT in preventing further visual loss in patients with occult CNV.[5,6]

Another randomized (not blinded) study of 26 patients did not find a statistically significant improvement for combination treatment with triamcinolone and TTT in comparison with TTT alone.[7] Results from available randomized controlled trials have contained methodological limitations and have failed to demonstrate a treatment benefit associated with TTT (over PDT). Nevertheless, the small sizes of many of these studies may not have allowed for the identification of a treatment difference where one truly existed due to lack of statistical power. Additional trials with larger numbers of patients are needed to establish the relative treatment effect associated with TTT.

Nonrandomized Studies

Several small non-comparative case series have been published on the use of TTT in patients with occult or classic subfoveal CNV secondary to AMD.[8-17] One small comparative trial has been reported as well.[18] However, interpretation of results from these studies is limited by the following:

- Results from small sample sizes limit the ability to rule out the role of chance as an explanation of study findings.[8-18]
- Lack of appropriate comparison group, which does not allow for conclusions regarding benefit of treatment over and beyond that offered by current medical standards.[8-17]
- Short-term (< 12 months) follow-up or lack of follow-up of primary health outcomes, which limits conclusions regarding net benefit of treatment.[8-10,12,16,19]

Some of these studies have raised questions concerning risk of complications (including macular burn) following the procedure and potential complications related to the limited ability to control rate and total amount of temperature applied during a procedure.[15,19,20]

Clinical Practice Guidelines and Position Statements

No evidence-based clinical practice guidelines were identified which recommend the use of TTT for the treatment of CNV.

American Academy of Ophthalmology (AAO)[21]

The 2013 AAO Preferred Practice Patterns (practice guidelines) on treatment of age-related macular degeneration recommend treatment of subfoveal CNV with intravitreal angiostatic agents (ranibizumab,

bevacizumab, or pegaptanib) or PDT.[22] The use of transpupillary thermotherapy is not addressed in the guideline.

Summary

The evidence is insufficient to determine whether transpupillary thermotherapy (TTT) for the treatment of choroidal neovascularization results in improved health outcomes. Although data from nonrandomized studies suggest there may be some improvement or stabilization in occult choroidal neovascularization, randomized controlled trials suggest there may be no treatment benefit. Additional randomized studies are needed to demonstrate that transpupillary thermotherapy improves health outcomes with acceptable levels of adverse effects over the natural course of the disease. Therefore, transpupillary thermotherapy is considered investigational.

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CROSS REFERENCES

Intraocular Radiation Therapy for Age-Related Macular Degeneration, Medicine, Policy No. 134

CODES	NUMBER	DESCRIPTION
CPT	67299	Unlisted procedure, posterior segment of eye

CODES	NUMBER	DESCRIPTION
HCPCS	None	