NATIONAL INSTITUTE FOR CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedures overview of transpupillary thermotherapy for age-related macular degeneration

Introduction

This overview has been prepared to assist members of the Interventional Procedures Advisory Committee advise on the safety and efficacy of an interventional procedure previously reviewed by SERNIP. It is based on a rapid survey of published literature, review of the procedure by specialist advisors and review of the content of the SERNIP file. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in December 2002

Procedure name

- Transpupillary thermotherapy for age-related macular degeneration.

Specialty societies

- *Royal College of Ophthalmologists.*

Description

Indications

Age-related macular degeneration is the most common cause of irreversible blindness in developed countries. The prevalence of macular degeneration rises with age, from about 0.7% in people aged 40 to 50 years, to 27% in people over the age of 90.[1] In 1996 there were 738,850 people older than 65 years of age registered blind or partially sighted in England. About 80%, or about 600,000, are likely to have age-related macular degeneration (Source: Royal National Institute for the Blind). The cause is unknown.

The macula is the part of the retina that provides central vision. Ninety per cent of people with age related macular degeneration have atrophic, or 'dry', macular degeneration, characterised by thinning of the macular retina. The other 10% have neovascular macular degeneration (also known as 'wet' or exudative macular degeneration). This type is characterised by the growth of new vessels in the choroid layer underneath the retina, which can threaten vision if they leak and cause scarring. The new vessels are described according to whether they can be seen clearly ('classic') or poorly ('occult') on a test called fluoroscein angiography. Occult

new vessels probably lie more deeply in the choroid than classic new vessels. New vessels in the foveal part of the choroid (subfoveal vessels) are potentially the most disabling, because the fovea is the central part of the macula, which is responsible for the sharpest vision. Wet macular degeneration usually occurs in people who already have dry macular degeneration.

The visual prognosis of wet macular degeneration is poor. Without treatment, 40% of people with occult neovascularisation develop severe visual loss within 2 years (www.rcophth.ac.uk). People with neovascularisation in one eye have about a 50% chance of developing a similar lesion in the fellow eye within 5 years.

Changes in visual acuity are usually measured by changes in the number of lines seen on a Snellen chart.

What the procedure involves

Lasers have been used for several years to coagulate new vessels in 'wet' macular degeneration. However, the procedure itself may permanently impair vision, especially if the vessels are very close to the fovea (subfoveal). Recurrence is common. Standard laser therapy uses a highly focussed beam and is only used, therefore, in classic neovascular macular degeneration, in which the target vessels are clearly visible. The technique is not used in people with occult new vessels.

Transpupillary thermotherapy uses laser energy to coagulate vessels in wet macular degeneration and is intended to alter the progression of the disease and preserve vision. This procedure uses a lower power, more diffuse beam than standard laser treatment. It may be used to treat occult new vessels.

Literature reviews

Appraisal criteria

All studies reporting clinical outcomes of transpupillary thermotherapy on patients with age-related macular degeneration were included.

List of studies found

No controlled studies were found.

Twelve case series were found. The five largest are described in the table.[1-5]

References to the seven smaller studies are given in the Appendix.

Table 1 Summary of key efficacy and safety findings (1)

Study details	Key efficacy findings	Key safety findings	Key reliability and validity issues
Ahuja[1] Retrospective case series USA 1999 to 2000 77 people (81 eyes) with occult new vessels, mean age 78, range 55 to 92) Inclusion criteria: • age > 50 • < 10% of lesion classic new vessels • < 50% subretinal haemorrhage Exclusion criteria: • no follow up data • allergic to fluorescein dye Mean follow up 9 months (range: 5-17)	Snellen acuity line change: • improved by 2 or more lines: 18 (22%) • stable: 38 (47%) • deteriorated by 2 or more lines: 25 (31%) Re-treatment rate: 30%	Macular infarction: 1 person	Uncontrolled retrospective case series. No self-rated patient outcomes. Follow up short.

Study details	Key efficacy findings	Key safety findings	Key reliability and validity issues
Algvere[2] Case series Stockholm, Sweden Published 2001 66 people (66 eyes) with predominantly occult new vessels • 38 occult, mean age 77 (range: 63-89) • 28 mixed (predominantly occult), mean age 78 (range: 59-88) 6 months follow up	Occult only: • Improved: 6 (16%) • Unchanged: 25 (66%) • Deteriorated: 7 (18%) Mixed: • Improved: 2 (7%) • Unchanged: 16 (57%) • Deteriorated: 10 (36%) (defined using objective score)	Postoperative haemorrhage: 3 eyes Postoperative increase of exudation: 4 eyes Progressive fibrosis: 6 eyes	Uncontrolled case series. No self-rated patient outcomes. No losses to follow up.

Study details	Key efficacy findings	Key safety findings	Key reliability and validity issues
Park[3] Retrospective case series Boston, USA 1996 to 2000 52 people (57 eyes), average age 77 Inclusion criteria: • mainly occult subfoveal new vessels • visual acuity of counting fingers or better • at least 4 month follow-up Exclusion criteria: • previously treated with surgery/laser therapy • predominantly serous pigment epithelial detachment or geographic atrophy Average follow up 10 months	Snellen acuity line change: • improved 2 or more lines: 10 (18%) • deteriorated three or more lines: 5 (9%)	9% eyes developed classic new vessels	Uncontrolled retrospective case series. No self-rated patient outcomes.. Follow up short.

Study details	Key efficacy findings	Key safety findings	Key reliability and validity issues
Kim[4] Retrospective case series Milwaukee, USA Published 2001 49 people with mainly occult subfoveal new vessels, mean age 78 (range: 60-96) Inclusion criteria: • ≥ 50 yrs • visual acuity < 20/40 • lesion consists of <25% haemorrhage • no obvious subretinal fibrous tissue • no prior laser treatment • no other pathology At least 12 weeks follow up; mean 7 months (range: 3–12)	3 month Snellen acuity line change: • improved 2 or more lines: 12 (25%) • deteriorated 1 or more line: 18 (38%) 6 month (available for 28 eyes) • improved 2 or more lines: 9 (32%), • deteriorated 1 or more lines: 12 (43%)	3 people developed large submacular haemorrhages in first 2 months	Uncontrolled retrospective case series. No self-rated patient outcomes. Follow up short.

Study details	Key efficacy findings	Key safety findings	Key reliability and validity issues
Newsom[5] Retrospective case series London, UK Published 2001 42 people (44 eyes), mean age: 78 • 12 predominantly classic • 32 predominantly occult inclusion criteria: • > 55 yrs Exclusion criteria: • previously treated • other serious ocular conditions Mean follow up 6.1 months (range: 2–19)	Snellen acuity line change: Predominantly classic: • improved more than 2 lines: none • deteriorated more than 2 lines: 4 people (33%) Predominantly occult: • improved more than 2 lines: 4 people (13%) • deteriorated more than 2 lines: 9 people (28%)	None reported	Uncontrolled retrospective case series. Not clear how long after treatment outcomes were measured.

Validity and generalisability of the studies

The studies were carried out in settings appropriate to the UK. All studies were relatively small uncontrolled case series. This study design is unreliable for establishing efficacy and safety of transpupillary thermotherapy compared with no treatment.

The majority of people included had occult or predominantly occult subfoveal new vessels. One study reported a small number of cases of classic or predominantly classic new vessels.[5]

Bazian comments

A multicentre randomised controlled trial comparing transpupillary thermotherapy with sham treatment began in March 2000 in the USA (Transpupillary Thermotherapy of Occult Subfoveal Choroidal Neovascular Membrane) (www.iridex.com/ophthalmology/clinical/3.html).

Specialist Advisor's opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College.

- Now established practice.
- Criteria for treatment and protocols are not yet well established.
- Inexpensive procedure, but may be significant cost implications for manpower and diagnostic services.
- Risk of unwanted thermal damage to retina.
- Technically straightforward.

Issues for consideration by IPAC

None other than those discussed above.

References

1. Ahuja, R. M., Benner, J. D., Schwartz, J. C., Butler, J. W., and Steidl, S. M. Efficacy of transpupillary thermotherapy (TTT) in the treatment of occult subfoveal choroidal neovascularization in age-related macular degeneration Seminars in Ophthalmology 2001; 16: 81-85

2. Algvere, P. V., Libert, C., and Seregard, S. Transpupillary thermotherapy of occult CNV with no or minimally classic CNV in age-related macular degeneration. Seminars in Ophthalmology 2001; 16: 90-96

3. Park, C. H., Duker, J. S., Mainster, M. A., Puliafito, C. A., and Reichel, E. Transpupillary thermotherapy (TTT) of occult choroidal neovascularization: A retrospective, noncomparative case series of fifty-seven eyes. Seminars in Ophthalmology 2001; 16: 66-69

4. Kim, J. E., Perkins, S. L., Schwiesow, T., Connor Jr, T. B., and Han, D. P. Transpupillary thermotherapy of occult choroidal neovascularization in age-related macular degeneration. Seminars in Ophthalmology 2001; 16: 86-89

5. Newsom, R. S., McAlister, J. C., Saeed, M., and McHugh, J. D. Transpupillary thermotherapy (TTT) for the treatment of choroidal neovascularisation. British Journal of Ophthalmology 2001; 85: 173-178

Appendix: Additional studies not included in the summary table

Reference	Number of study participants
Karel, I., Zahlava, J., Boguszakova, J., Dubska, Z., and Lestak, J. Transpupillary thermotherapy in age-related macular degeneration. Preliminary results. [Czech] *Ceska a Slovenska Oftalmologie* 2002; 58: 215–23	35
Friberg, T. R., Pandya, A., and Nazari, K. Transpupillary thermotherapy (TTT) for age-related macular degeneration. *Seminars in Ophthalmology* 2001; 16: 70–80	35
Thompson, J. T. Retinal pigment epithelial tear after transpupillary thermotherapy for choroidal neovascularization. *American Journal of Ophthalmology* 2001; 131: 662–4	25 eyes
Beintema, M. R., Oosterhuis, J. A., and Hendrikse, F. Yellow dye laser thermotherapy of choroidal neovascularisation in age related macular degeneration. *British Journal of Ophthalmology* 2001; 85: 708–13	24 eyes
Gaun, S., Tateiwa, H., Arai, J., Kuroiwa, S., et al. Transpupillary thermotherapy for choroidal neovascularization in age-related macular degeneration. Japanese Journal of Clinical *Ophthalmology* 2002; 56: 715–9	17 eyes
Reichel, E., Berrocal, A. M., Ip, M., Kroll, A. J., et al. A. Transpupillary thermotherapy of occult subfoveal choroidal neovascularization in patients with age-related macular degeneration. *Ophthalmology* 1999; 106: 1908–14	15 eyes
Nehemy, M., Passos, E., Campos, C., Rodrigues, R. P., et al. Indocyanine green enhanced transpupillary thermotherapy of choroidal neovascularization caused by age-related macular degeneration. *Revista Brasileira de Oftalmologia* 2001; 60: 251–9	4 eyes