Photodynamic therapy for age-related macular degeneration

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Photodynamic therapy is a new treatment modality for wet age-related macular degeneration (ARMD). GPs need to know when to refer suitable patients, as well as how to advise them on what is involved in treatment and the potential outcomes to be expected.

What is ARMD?

Age-related macular degeneration (ARMD) is a progressive disease of the central retina that results in deterioration of the central visual field. It affects approximately 2% of the population over 50 years of age, increasing to 18.5% among those 85 years of age or older.[1]

The two types of ARMD are 'dry' (90% of cases) and 'wet' (10% of cases). The peripheral retina in both types tends to be spared, preserving side vision and therefore maintaining ambulatory vision.

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Dry ARMD

Dry ARMD is characterised by drusen, pigmentary changes and atrophy of the macular region. Patients may notice a slow deterioration of their vision, particularly for reading and fine work.

Wet ARMD

Wet ARMD is characterised by the growth of abnormal blood vessels into the retina resulting in a neovascular membrane. Patients complain of a recent onset of distortion of their vision, such as seeing wavy lines.

The natural history for an untreated neovascular membrane is to enlarge and haemorrhage (Figure 1). This eventually involves an extensive area of the macula, resulting in total loss of central vision.

What is photodynamic therapy?

Photodynamic therapy is a recently developed treatment for the wet type of ARMD. Its advantage is that it can destroy the abnormal blood vessels without causing thermal damage to the surrounding normal retina. Photodynamic therapy is not effective for the dry type of ARMD.

The dye used in the treatment, verteporfin (Visudyne), binds to low density lipoprotein (LDL) in the bloodstream. The neovascular membrane has higher levels of LDL receptors than normal vascular tissue and binds the verteporfin–LDL complexes. Nonthermal red laser light at a wavelength of 689 nm is applied to the membrane – this activates the release of oxygen free radicals and results in endothelial damage, thrombus formation and occlusion of the abnormal vessels.

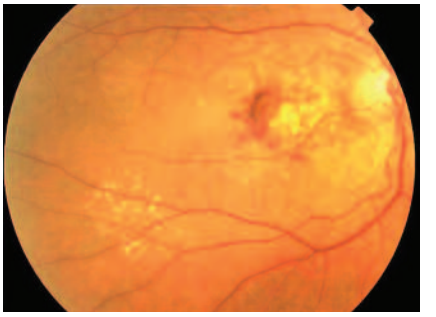


Figure 1. A colour photograph showing a neovascular membrane with associated haemorrhage.

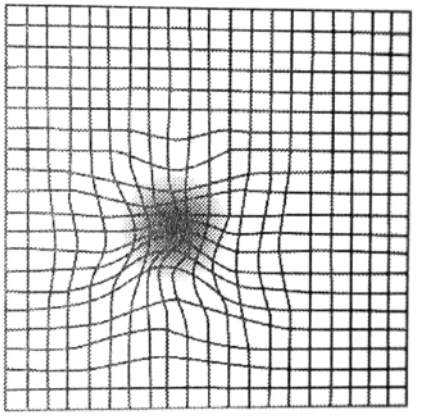


Figure 2. An Amsler grid, which consists of a square grid of horizontal and vertical lines, as seen by a patient with wet ARMD. The area of distortion represents the region of the macula involved.

The aim of treatment is to stabilise the current level of vision by confining and inhibiting the progression of the neovascular membrane. The success rate for stabilisation is approximately 70%.

How is suitability for treatment assessed?

An Amsler grid can be used to determine the presence of a macular lesion. In patients with wet ARMD, the lines on the

grid appear wavy or missing (Figure 2). The area of distortion corresponds with the affected region.

A fundus fluorescein angiogram performed by an ophthalmologist is used to identify the location and size of the neovascular membrane. Fluorescein dye (3 to 5 mL) is injected into a peripheral vein and circulates to the retinal vessels; these can be photographed using a special camera (Figure 3a). A neovascular membrane is seen as a bright area that represents an area of dye leakage. The type (classic or occult), location (subfoveal or extrafoveal) and size of the membrane can be determined, and the decision on whether to proceed with photodynamic therapy can be made.

What does the procedure involve?

Photodynamic therapy is a two-step process. The first step involves a 10-minute infusion of the verteporfin dye via a peripheral vein. Five minutes after the infusion is complete, local anaesthetic is placed in the eye and a contact lens applied that focuses the laser onto the retina. The low intensity laser is shone into the eye to activate the verteporfin in the neovascular membrane.

Multiple treatments are required to achieve this goal. A fundus fluorescein angiogram is repeated at six to eight weeks to assess the remaining activity of the abnormal blood vessels and the need for any further treatment (Figure 3b). On average, three or four treatments are required in the first year.

Patient information about photodynamic therapy is provided in the box on page 82.

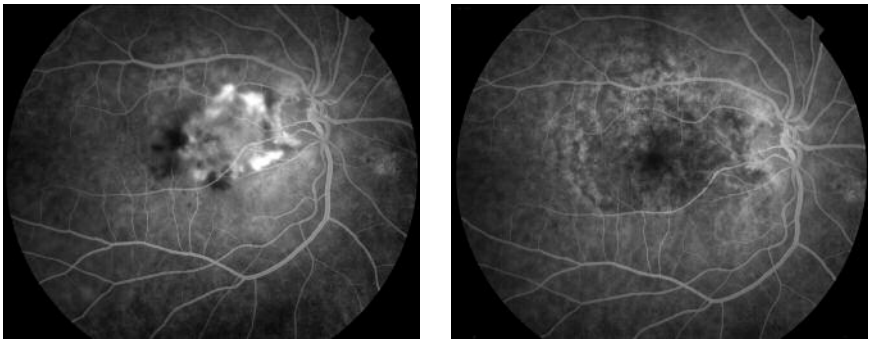
What are the side effects?

Adverse reactions to photodynamic therapy may include skin reactions at the injection site, blurred vision and visual defects. Approximately 3% of patients have transient back pain related to the infusion, but ceasing shortly after it is terminated. Approximately 20% of patients incur mild to moderate visual disturbances – these are mostly of a transient nature.

What about postoperative care?

After administration of photodynamic therapy, the patient's skin and eyes will be sensitive to light for three days. Patients should be instructed to avoid exposure to direct sunlight for three days otherwise severe sunburn could result.

Patients are given an Amsler grid that they can use to check for any changes in their vision and thereby contact their doctor for urgent review. There is a high risk of the other eye developing wet ARMD, so it is important that any new development of a membrane is diagnosed and treated as early as possible to minimise vision loss.



Figures 3a (left) and b (right). Fundus fluorescein angiograms performed before (a) and after (b) photodynamic therapy for wet ARMD. Reduced leakage from the neovascular membrane is seen after treatment.

What is the cost of photodynamic therapy?

Photodynamic therapy is expensive: for private patients, the cost of the verteporfin dye alone is about $2000 per treatment and a fundus fluorescein angiogram needs to be performed prior to each session. Since 1 July 2002, the Australian Government has approved a Medicare rebate for the procedure, based on an individual's level of vision (6/60 or better), the position of the membrane (subfoveal), type of membrane (classic) and number of treatments that he or she has undertaken. The ophthalmologist will be able to provide advice regarding a patient's eligibility for the rebate. Currently, the Department of Veterans Affairs covers the full cost for gold card holders.

What other management options are available?

Argon laser ablation

An argon laser can be used to burn the abnormal blood vessels, which will limit the size of the membrane. However, the surrounding retina will also be destroyed, resulting in immediate loss of central vision.

Transpupillary thermoplasty

Transpupillary thermoplasty is a different type of laser treatment for wet ARMD. This procedure involves heating of the abnormal vessels while sparing the overlying retina.

Transpupillary thermoplasty is a useful, less expensive alternative to photodynamic therapy, but is associated with a lower rate of success (approximately 50% closure of the abnormal vessels). Like photodynamic therapy, this laser treatment generally needs to be repeated.

Supplements

A combination of vitamins A, C and E, zinc and copper has been found to slow the progression of wet ARMD. However, it is uncertain whether this is of benefit in early disease.[2]

Notes for patients undergoing photodynamic therapy

This handout has been designed to help you understand age-related macular degeneration (ARMD) and photodynamic therapy. If you have questions after reading this information, be sure to ask your doctor.

What is ARMD?

ARMD is a progressive disease that reduces central vision, which is the vision needed for activities such as reading, driving and seeing faces. There are two types of ARMD – 'wet' and 'dry'. The disease affects the retina, the light sensitive tissue that lines the back of the eye.

What is photodynamic therapy?

Photodynamic therapy is a recently developed procedure that uses a laser to treat the wet type of ARMD with the aim of preventing a further decline in vision. It is not effective for the dry type of ARMD.

How do I prepare for photodynamic therapy?

On the day you are to receive photodynamic therapy, bring the following items to the doctor's office: dark sunglasses, gloves, a wide-brimmed hat, a long-sleeved shirt and slacks. You will need to reschedule any dental or other appointments that use bright halogen lighting until at least three days after treatment (the light sensitive period).

What does the treatment involve?

Before the procedure, your pupil will be dilated so that the doctor can visualise the retina in the back of your eye. You will be given an infusion of a light activated drug called verteporfin (Visudyne) via a vein in your arm. This takes 10 minutes. Five minutes after completing the infusion, the doctor will instil an eyedrop to numb the surface of your eye, and a contact lens will be placed on the cornea. This lens acts to focus light on the retina and also keeps the eyelids open. The laser will then be shone onto the affected area of the retina for 83 seconds. The laser activates the drug within the abnormal blood vessels, causing them to close. The laser does not cause any heating so it does not burn.

What are the side effects of treatment?

The side effects of photodynamic therapy can include skin reactions at the injection site, back pain during the infusion, and blurred vision following the treatment. Your doctor may be consulted if you experience any of these conditions after photodynamic treatment.

What do I do after the treatment?

After each treatment, you should avoid exposure to direct sunlight or bright light for three days or as directed by your doctor. Be sure if you are near a window in your home during daytime that you have curtains or shades drawn to block out direct sunlight and that you avoid direct sunlight from skylights. If you really need to go out during daylight hours within the light sensitive period, wear a long-sleeved shirt and pants (preferably tight-knit), gloves, socks and shoes, sunglasses and a wide-brimmed hat. Other sources of bright light should also be avoided, including tanning salons and halogen lighting in homes and offices (such as bright halogen reading lamps).

You should not, however, stay in the dark during the light sensitive period. Exposing your skin to indoor light will help to inactivate the drug in the skin. You can watch TV or go to the movies but, if possible, wait until sunset to do outside chores or shopping. Note that UV sunscreens are not effective in protecting against photosensitivity reactions. After the light sensitive period, you may resume normal outdoor activities without any special precautions.

What about follow up?

Six to eight weeks following your first treatment, your doctor will ask you to return for a follow up photograph of the retina. The need for further laser treatment is based on the remaining activity of the neovascular membrane (abnormal blood vessels in the retina). Patients generally require multiple treatments – on average, three or four in the first year.

As the ageing process is ongoing, there is a future risk of recurrence of wet ARMD and so lifelong follow up is recommended. You will be given an Amsler grid to monitor your vision at home. If any new distortion is noted in either eye, urgent review by an ophthalmologist is recommended.

Where can I get further information?

Your ophthalmologist will be able to provide further information about ARMD and photodynamic therapy. He or she can provide you with a pamphlet, 'A patient's guide to Visudyne (verteporfin) therapy', which is produced by Novartis Ophthalmics (manufacturer of Visudyne).

This patient handout was prepared by Dr G.A. Lee and Dr L.R. Lee.

Conclusion

Photodynamic therapy is a recent technology proven to be beneficial in slowing the progression of wet ARMD. The success rate for stabilising vision is around 70%. It is a valuable treatment, and needs to be performed over multiple sessions. Further research is underway to determine the long term effectiveness of photodynamic therapy and to develop other forms of treatment. MT

References

1. Mitchell P, Smith W, Attebo K, Wang JJ. Prevalence of age-related maculopathy in Australia. The Blue Mountains Eye Study. Ophthalmology 1995; 102: 1450-1460.
2. A randomized, placebo-controlled, clinical trial of high-dose supplementation with vitamin C and E, beta carotene, and zinc for age-related macular degeneration and vision loss: ARED report no. 8. Arch Ophthalmol 2001; 119: 1417-1436.

Further reading

1. Guymer R. Drug treatment for macular degeneration. Aust Prescr 2002; 25: 116-119.