Half dose verteporfin PDT for central serous chorioretinopathy

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Tailoring the therapy to the disease

Obtaining the maximum treatment effect with minimal toxicity is a guiding principle of dosing in pharmacology and medicine. In managing patients with central serous chorioretinopathy (CSC), clinicians have traditionally chosen between two options: observation and thermal laser therapy. The fact that laser damages the retinal pigment epithelium (RPE) in the setting of a disease with a known risk of developing choroidal neovascularisation (CNV) has left clinicians seeking new treatments that are both more effective and less toxic.

Recently, various groups have reported that photodynamic therapy (PDT) can be an effective treatment for the serous exudation of CSC.¹⁻⁴ This approach is based on the notion that choroidal hyperpermeability, as demonstrated by indocyanine green angiography, is an underlying contributor to subretinal and sub-RPE fluid accumulations in CSC. The presumed therapeutic mechanism of action of PDT in these cases is closure of vascular channels in the choriocapillaris.¹ An undesired effect of verteporfin PDT in CSC, however, can be pigmentary RPE changes in the treatment zone and persistent hypoperfusion of the choriocapillaris as identified with ICG angiography.⁴

In this issue of *BJO* (p 869), Lai and co-workers describe a new strategy for treatment of CSC.⁵ Using a reduced dose of verteporfin, they found that some benefit can be achieved safely with PDT. Their rationale was that using less drug might reduce the amount of collateral RPE damage from the treatment. In this uncontrolled series, a group of patients with chronic CSC and relatively good vision (median 20/40) received PDT with half the standard verteporfin dose, a faster infusion time, and a shorter drug light interval. Most patients had improvement of vision, retinal thickness, and serous detachment.

The pretreatment vision in this series highlights an important difference between CSC and age related macular degeneration (AMD), for which verteporfin PDT is commonly used. In AMD, patients undergoing this treatment

often have poor vision to start with. In CSC, patients, such as those studied in this series, may have a lower threshold for noticing side effects of the treatment. It is not known yet whether vision suffers in the long term when RPE disturbances result from PDT treatments. Seen in this light, CSC with its predilection for the young is an especially important disease in which to optimise the verteporfin PDT protocol so as to avoid unnecessary choroidal and RPE damage.

Administering verteporfin PDT with parameters other than those used in the TAP study is not a new concept. In choroidal haemangioma, for example, multiple groups have reported success with a bolus injection of verteporfin followed by photoactivation,^{6,7} while others have shown that the TAP treatment parameters can be effective in this disease. (Bolus infusion of verteporfin has also been used successfully in AMD associated CNV.⁸) The emerging literature on haemangioma treatment has demonstrated that the clinical end point of shutting down circulation may be achieved by PDT delivered in various ways.

Only head to head comparisons can show whether one treatment method is better than another

An important lesson from the experience with haemangiomas is that varying the verteporfin dose is not the only way to try to achieve a safer treatment. Fluence and the time course of delivery are important variables to be optimised. This was not addressed in a systematic way in the present study by Lai and co-workers and is thus a major item of unfinished business from their work. Others have shown that in patients with AMD, reducing the fluence can result in less choriocapillaris damage.⁸ In the VIM study, two different fluence settings were used in treating CNV, but the study was not powered to determine whether one was better than the other.⁹

How much improvement can be expected in treating CSC patients with PDT? Lai and co-workers in the present

study found a median visual improvement of only one line at 1 month in their patients with chronic CSC treated with half dose verteporfin—but the average starting vision was already good, making it difficult to record dramatic improvements. The OCT findings did improve in most patients in the series. Although the apparent effectiveness for vision in this small series may leave something to be desired, the main value of this study is that it reminds us to “think outside the box” of the standard PDT treatment parameters, especially when using PDT for indications other than those studied in TAP. Larger trials for CSC might provide more dramatic visual improvement data.

Looking ahead, it may be that as our experience grows, we will begin to tailor the dose, fluence, and other variables in the PDT treatment protocol for each specific case, depending on the indication for treatment. Perhaps even among patients with a particular diagnosis, we will be able to individualise the treatment according to the features of the disease process (for example, varying the dose or time course of delivery in occult versus classic CNV, or in CSC with serous retinal detachment versus RPE detachment). Only head to head comparisons can show whether one treatment method is better than another, but Lai and co-workers are helping to move us in that direction. Their study provides further “proof of principle” for varying parameters including the drug dose—but, for example, does not show whether a half dose is better than a third or two thirds dose. To further complicate matters, combination therapies have become more common recently in AMD (for example, verteporfin PDT plus intravitreal steroid injection). We may find that certain combinations work better with different PDT parameters depending upon the nature of the disease process.

It should be noted that the present study does not resolve the question of whether CSC is better left alone or treated. Nevertheless, in the event that a clinician favours treatment, it is important to know which intervention is safest and most effective. Lai and colleagues have taken us a step closer to that goal.

Br J Ophthalmol 2006;**90**:805–806.
doi: 10.1136/bjo.2006.093328

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