Photodynamic therapy for wet age-related macular degeneration

Clinical effectiveness and cost–utility of photodynamic therapy for wet age-related macular degeneration: a systematic review and economic evaluation

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Executive summary

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Executive summary

Background

Age-related macular degeneration (AMD) is a major cause of blindness affecting the central portion of the retina (the macula). Wet AMD is one form of the condition and involves the formation of neovascular membranes. It is through the leakage and bleeding of these blood vessels that vision loss, which is usually irreversible, occurs. Wet AMD can be further subdivided into classic and occult and it is the classic form that is more threatening to sight. The prevalence of wet AMD has been estimated at 3 per 1000 at age 60–64 years and 117 per 1000 at 90 years and over. There are approximately 50 new cases of classic neovascular membranes per year in a typical health authority of population 500,000.

Photodynamic therapy (PDT) is a new intervention that uses photosensitive drugs (e.g. verteporfin) and a specially developed low-powered laser, and is intended to treat patients with new neovascular membranes in wet AMD who still retain some visual acuity. Its aim is to stop further loss of vision rather than restore vision already lost.

Objective

- To establish the clinical and cost-effectiveness of PDT for the neovascular form of wet AMD relative to current practice and in relation to current licensed indications.

Methods

A systematic review of randomised controlled trials (RCTs) and economic evaluations addressing the clinical effectiveness and cost–utility of PDT in AMD was undertaken. Searches in electronic databases, health technology assessment Internet sites, reference lists from publications, conference abstracts and the Novartis Industry Submission to the National Institute for Clinical Excellence for completed and ongoing RCTs and for economic evaluations, were carried out up to August/September 2001. Decisions on the inclusion or exclusion of RCTs and economic evaluations were made by one reviewer, independently of results, and checked by another. Duplicate data extraction and quality assessment were carried out using predefined criteria. Synthesis was mainly qualitative for both clinical effectiveness and cost–utility. Forest plots were carried out for the RCT primary outcome measure of clinical effectiveness. A health economist, taking a public finance perspective and using a simple decision model, carried out a cost–utility analysis for this report. PDT with best supportive care was compared with best supportive care only, using clinical effectiveness data from one RCT, published utility and treatment cost studies and blindness cost estimates.

Results

Number and quality of studies, and direction of evidence

In the Treatment of Age-related Macular Degeneration with Photodynamic Therapy (TAP) trial there was consistent evidence at both 1 and 2 years that verteporfin PDT results in less deterioration in visual acuity in the randomised eye than placebo. The relative risk for loss of 15 letters (three lines) or more at 2 years was 0.75 (95% confidence interval (CI), 0.65 to 0.88). This effect is both statistically significant and clinically important. The Verteporfin in Photodynamic Therapy (VIP) trial showed a similar result. There is an increase in adverse events associated with verteporfin PDT. Most are minor, but sudden visual loss occurs in 1.0–4.4% of verteporfin PDT patients and is an effect that patients should be aware of.

Summary of benefits

The balance of beneficial and disbeneficial effects measured in the included RCTs appears to favour verteporfin PDT. However, avoiding deterioration in visual acuity, does not equate directly with improving patient function and quality of life. Also, function is dependent on vision in both eyes, not just the impact of wet AMD on one eye and this needs to be taken into account. Lack of heterogeneity between the results of TAP and VIP invites re-examination of the assumption that the nature of the wet AMD neovascular lesions has as much influence on

the relative effect of verteporfin PDT as is predicted on the basis of an assessment of clinical heterogeneity. Further investigation suggests the results of subgroup analyses should be treated with extreme caution and at best should be regarded as generating hypotheses requiring more research. The impact of reduced deterioration in visual acuity should be based on whole trial estimates of effect.

Economic analysis

Costs

The cost of one vial of verteporfin is currently £850. The current treatment costs for PDT treatment were estimated at £1181 per treatment. The net cost impact of implementing verteporfin PDT to the NHS for its currently licensed indication is between £16.4 million and £41.3 million per annum by the third year of the service being introduced. This figure could increase to £63.4 million by the third year if the licence was extended to all wet AMD neovascular lesions. These figures do not include the costs of training and likely need for increased numbers of consultant ophthalmologists and other trained staff.

Cost/quality-adjusted life-year

There is uncertainty about the cost–utility of verteporfin PDT. Cost-effectiveness studies reviewed estimated that the cost per quality-adjusted life-year at 2 years ranged from £60,000 to £122,000. The economic model developed as part of this report obtained a base-case estimate of between £151,000 and £182,000. The sensitivity analyses ranged from the best scenario of £47,000 to a worst scenario of £342,000. All of the estimates at 2 years are at best at the margins of what is generally considered to be an efficient use of health-care resources. None of them take into account that wet AMD can occur in the worse-seeing eye. More favourable estimates of cost–utility have only been obtained in models extrapolating beyond 2 years, the limit of RCT data.

Conclusions

Need for further research

There is a need to conduct a large, multicentre, publicly funded pragmatic double-blind RCT with parallel health economic evaluation to assess not just the impact of PDT on visual acuity and adverse events, but also directly measured global quality of life and survival. There is no indication of the relationship between benefits and costs where wet AMD affects the worse-seeing eye first. Treatment of wet AMD, with verteporfin, other types of PDT, and other new technologies is an area under very active investigation, so this technology should be kept under close review.

Publication

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The research reported in this monograph was commissioned by the HTA Programme on behalf of the National Institute for Clinical Excellence (NICE). Technology assessment reports are completed in a limited time to inform the appraisal and guidance development processes managed by NICE. The review brings together evidence on key aspects of the use of the technology concerned. However, appraisals and guidance produced by NICE are informed by a wide range of sources.

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