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Rapid review

Executive summary

Combination therapy (interferon alfa and ribavirin) in the treatment of chronic hepatitis C: a rapid and systematic review

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Executive summary

Background

Hepatitis C is a viral disease of the liver, which frequently causes few or no symptoms at first infection but has a high probability of becoming an insidious chronic disease. Treatment has traditionally been with interferon alfa but only a small proportion of patients have been cured by this method. The recent introduction of ribavirin, given in combination, has led to a re-appraisal of the management of chronic hepatitis C.

The current report considers the additional benefit of combination therapy (interferon alfa and ribavirin) compared with monotherapy (interferon alfa alone) for the treatment of patients with chronic hepatitis C. It supersedes two reports of combination therapy conducted by the Scottish Health Purchasing Information Centre and the Wessex Institute for Health Research and Development.

Objective

To review the clinical effectiveness and cost-effectiveness of combination therapy with interferon alfa and ribavirin in patients with chronic hepatitis C.

Methods

Effectiveness

Electronic databases were searched from 1993 to the end of 1999, to identify randomised controlled trials (RCTs) or systematic reviews of RCTs that evaluated interferon alfa in combination with ribavirin compared with interferon alfa alone (or placebo) in patients with chronic hepatitis C. Bibliographies from previous studies were also examined.

Economic analysis

The economic evaluation is based on the three largest RCTs of combination therapy, and a pooled analysis of two of these trials. Sustained virological response rates were entered into a spreadsheet model incorporating a hypothetical cohort of 1000 patients who were followed over a 30-year period.

Results

Effectiveness

Nineteen RCTs and two meta-analyses were identified. The methodological quality of the included studies was variable, though the larger RCTs and meta-analyses were considered to be of high quality. Results of these trials indicate that combination therapy produces larger sustained response rates than monotherapy. For patients naïve to interferon treatment, sustained virological response rates were: 33% (95% confidence interval (CI), 29 to 37) for combination therapy compared with 6% (95% CI, 3 to 10) for monotherapy, based on 24 weeks of treatment; and 41% (95% CI, 36 to 45) compared with 16% (95% CI, 13 to 19), respectively, for 48 weeks of treatment. For patients who had relapsed following a previous course of interferon, sustained virological response rates were 49% (95% CI, 42 to 57) compared with 5% (95% CI, 2 to 9), respectively, based on 24 weeks of treatment.

Two groups of chronic hepatitis C patients are expected to benefit from combination therapy: interferon-naïve patients and relapse patients.

Economic analysis

A 4-week cycle of interferon alfa at 3 mU three times a week costs £194; ribavirin costs £543. Thus, ribavirin substantially increases drug costs compared with interferon monotherapy. Six months of combination therapy will cost £4422 (excluding monitoring costs).

For interferon alfa-naïve patients, the **additional** discounted cost per quality-adjusted life-year (QALY) gained from treatment with combination therapy for 6 months compared with no active treatment is £7578. For patients who have relapsed after a previous course of interferon alfa, the **additional** discounted cost per QALY gained from treatment with combination therapy for 6 months compared with monotherapy for 6 months is £3503.

A subgroup analysis was conducted to examine the sensitivity of the cost per QALY based on the response rates of different patient subgroups (chronic hepatitis C patients with between none

and five favourable response factors). This shows it is worth treating all patients with combination therapy as first-line treatment for 6 months, but only worth treating those with one or two response factors for a further 6 months. Those with three or four factors do well by 6 months, but gain very little from further treatment (cost per QALY is approximately £150,000). Those with no favourable response factors do badly with 6 months of treatment – only 8% responded by 6 months, and further treatment is not cost-effective (cost per QALY of approximately £300,000).

Conclusions

There is benefit associated with combination therapy and treatment can be cost-effective. It is appropriate to offer 6 months of combination therapy as first-line treatment to patients not previously treated with interferon and also to patients who have relapsed following a previous course of interferon. At 6 months, continuation of treatment should depend on factors that may predict a good sustained response.

Uncertainties

Variations in the prevalence of hepatitis C virus mean that the cost of combination therapy would vary considerably among health authorities; for example, areas with significant drug abuse problems might sustain higher total costs than areas where drug abuse is not a big problem, though compliance among users to attend for treatment and to stop injecting is known to be poor.

The rate of progression of hepatitis C is very slow and, at present, knowledge of the natural history of the disease is incomplete. There is uncertainty about the benefits of treating patients with mild disease and few or no symptoms. Trials are underway.

Publication

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NHS R&D HTA Programme

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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). Rapid reviews are completed in a limited time to inform the appraisal and guideline development processes managed by NICE. The review brings together evidence on key aspects of the use of the technology concerned. However, appraisals and guidelines produced by NICE are informed by a wide range of sources.

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