Health benefits of antiviral therapy for mild chronic hepatitis C

Health benefits of antiviral therapy for mild chronic hepatitis C: randomised controlled trial and economic evaluation

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Executive summary

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Executive summary

Objectives

The objectives of the study were to determine whether combined therapy with interferon-α and ribavirin was more effective and cost-effective than no treatment for patients with mild chronic hepatitis C.

Methods

Design and setting

A multicentre, randomised, controlled, non-blinded trial (RCT) assessed the efficacy of combination therapy. A Markov model used these efficacy data combined with data on transition probabilities, costs and health-related quality of life (HRQoL) to assess the lifetime cost-effectiveness of the intervention.

Participants

Treatment-naive, adult patients with histologically mild chronic hepatitis C (Ishak necroinflammatory scores <4 and fibrosis scores <3 on liver biopsy).

Intervention

Participants were randomised to receive interferon-α and ribavirin for 48 weeks or no treatment (control).

Main outcome measures

The primary outcome measure was the proportion of patients having a sustained virological response (SVR), measured at 6 months after cessation of therapy. Secondary outcome measures were: the ability of early phase kinetics to predict the eventual outcome of treating mild disease; HRQoL measured using the Short Form 36 and EuroQol (5 Dimensions) questionnaires, and the cost per quality-adjusted life-year (QALY) of interferon-α and ribavirin for mild disease compared with no treatment.

Results

In the treatment group, 32 out of 98 patients (33%) achieved an SVR. Patients infected with genotype 1 had a lower SVR than those infected with genotype non-1 (18% versus 49%, $p = 0.02$). No patients who failed to achieve a 2-log drop in viral load at 12 weeks achieved an SVR. HRQoL fell during treatment and rose with treatment cessation. For patients having an SVR there were modest improvements in HRQoL at 6 months post-treatment. The mean cost per QALY gained was £4535 for 40-year-old patients with genotype non-1 and £25,188 for patients with genotype 1. For patients with genotype 1 aged 65, providing interferon-α and ribavirin for mild disease led to fewer QALYs gained, and a mean cost per QALY of £53,017. The model using efficacy estimates from the literature, showed that the cost per QALY gained from providing pegylated interferon α-2b and ribavirin at a mild stage rather than a moderate stage was £7821 for patients with genotype non-1 and £28,409 for patients with genotype 1.

Conclusions

Implications for healthcare

Based on the evidence collected in this study, interferon-α and ribavirin treatment for mild chronic hepatitis C patients with genotype non-1 is effective, and in general cost-effective at the £30,000 per QALY threshold previously used by policy-makers in the NHS. For patients with chronic hepatitis C aged 65 or over with genotype 1, antiviral treatment at a mild stage does not appear cost-effective.

Recommendations for research

- For patients with genotype 1 the estimates of cost-effectiveness were sensitive to the gain in HRQoL following an SVR. Further research is required to investigate the long-term HRQoL for genotype 1 patients who have had an SVR.
- To provide a full assessment of the cost-effectiveness of pegylated interferon-α and ribavirin at a mild compared with a moderate stage, research is needed to assess the impact of pegylated interferon-α and ribavirin on SVRs, HRQoL and health service costs.
- The use of predictive tests based on pharmacogenomics to target therapy to those most likely to respond should now be developed.

- For patients with mild hepatitis C liver biopsy before treatment no longer appears justified apart from for older patients (aged 65 or over) with genotype 1. However, further research should monitor the impact this strategy would have on costs and outcomes.

Publication

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NHS R&D HTA Programme

The research findings from the NHS R&D Health Technology Assessment (HTA) Programme directly influence key decision-making bodies such as the National Institute for Health and Clinical Excellence (NICE) and the National Screening Committee (NSC) who rely on HTA outputs to help raise standards of care. HTA findings also help to improve the quality of the service in the NHS indirectly in that they form a key component of the 'National Knowledge Service' that is being developed to improve the evidence of clinical practice throughout the NHS.

The HTA Programme was set up in 1993. Its role is to ensure that high-quality research information on the costs, effectiveness and broader impact of health technologies is produced in the most efficient way for those who use, manage and provide care in the NHS. 'Health technologies' are broadly defined to include all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care, rather than settings of care.

The HTA Programme commissions research only on topics where it has identified key gaps in the evidence needed by the NHS. Suggestions for topics are actively sought from people working in the NHS, the public, service-users groups and professional bodies such as Royal Colleges and NHS Trusts.

Research suggestions are carefully considered by panels of independent experts (including service users) whose advice results in a ranked list of recommended research priorities. The HTA Programme then commissions the research team best suited to undertake the work, in the manner most appropriate to find the relevant answers. Some projects may take only months, others need several years to answer the research questions adequately. They may involve synthesising existing evidence or conducting a trial to produce new evidence where none currently exists.

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Reports are published in the HTA monograph series if (1) they have resulted from work commissioned for the HTA Programme, and (2) they are of a sufficiently high scientific quality as assessed by the referees and editors.

Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search, appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

The research reported in this monograph was commissioned by the HTA Programme as project number 95/24/03. The contractual start date was in August 1998. The draft report began editorial review in June 2004 and was accepted for publication in February 2005. As the funder, by devising a commissioning brief, the HTA Programme specified the research question and study design. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

The views expressed in this publication are those of the authors and not necessarily those of the HTA Programme or the Department of Health.

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