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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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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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.

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