Optimal length of antiviral therapy in patients with hepatitis C virus genotypes 2 and 3: a meta-analysis

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CRD summary
This review found no difference in efficacy between shorter (12 to 16 weeks) and longer (24 weeks) treatment with pegylated interferon and ribavirin for hepatitis C virus genotype 2 and 3 patients who achieved rapid virological response after four weeks. The conclusions should be treated with caution because details about review methods were lacking and heterogeneity between studies was high.

Authors' objectives
To compare the efficacy of short and standard duration antiviral therapy in patients with hepatitis C virus genotypes 2 and 3.

Searching
MEDLINE, Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science and ClinicalTrials.gov were searched for articles published in English between 2000 and October 2008. Search terms were reported.

Study selection
Randomised controlled trials (RCTs) that evaluated standard pegylated interferon and ribavirin combination therapy in adults with hepatitis C virus genotypes 2 and 3 that compared short (12 to 16 weeks) with standard (24 weeks) therapy were eligible for inclusion. Use of standard combination therapy had to be similar in both arms and studies had to report sustained virological response rates.

The included studies either randomised patients to short and standard treatment durations at baseline or after rapid virological response was achieved. Outcomes of interest were sustained virological response (defined as a negative result on a qualitative PCR assay six months after the end of treatment), rapid virological response (defined as a negative assay results four weeks after the start of treatment) and end of treatment (defined as a negative assay result after termination of treatment). All studies gave pegylated interferon (types varied) with between 800mg and 1,400mg of ribavirin per day (depending on body weight). Short treatment durations ranged from 12 to 16 weeks. Mean patient age ranged from 38 to 50.2 years. Between 60% and 81% of patients were male. Between 20% and 100% of patients were genotype 2.

Studies were selected independently by two reviewers. Disagreements were resolved by discussion.

Assessment of study quality
Study quality was assessed using the Jadad scale of randomisation sequence, double blinding and the reporting of withdrawals (maximum possible score of 5).

The authors did not report how many reviewers performed the quality assessment.

Data extraction
Data on the types, doses and duration of treatment and outcome rates were extracted. Authors were contacted for clarification of missing data. Outcome rates were used to calculate relative risks (RR) with 95% confidence intervals (CI).

The authors did not report how many reviewers performed the data extraction.

Methods of synthesis
Results were pooled using a random-effects meta-analysis on an intention-to-treat basis. Additional analyses excluded results from studies that were published as abstracts only and those that compared the two randomisation timings. Heterogeneity was assessed using $X^2$ and $I^2$. Numbers needed to treat (NNT) were calculated from the pooled results. Publication bias was assessed using funnel plots and regression tests.

**Results of the review**

Eight RCTs (n=2,786 patients) were included. All trials were open label. One trial was double-blind only up to 16 weeks of treatment. All trials described dropouts. The maximum quality score was 3 (out of 5).

**Sustained virological response:** Sustained virological response rates were lower in patients who received a shorter duration of treatment compared with standard, but the comparison was not statistically significant. The number needed to treat was 94. Heterogeneity was high ($I^2=86\%$). There appeared to be no evidence of publication bias. Subgroup analyses of three trials with baseline randomisation, and five that randomised patients at rapid virological response showed very similar results for both groups. Pooling of only full-text papers resulted in a similar conclusion.

**End of treatment:** There was no statistically significant difference between short and standard duration of treatment in end of treatment rates, based on three trials.

**Authors' conclusions**

For hepatitis C virus genotype 2 and 3 patients who achieved rapid virological response after four weeks, there was no difference in efficacy between a shorter (12 to 16 weeks) and longer (24 weeks) duration of treatment with pegylated interferon and ribavirin.

**CRD commentary**

This review had clearly stated inclusion criteria for study design, interventions, participants and outcomes. Restricting the search to studies published in English increased the risk of language bias. Publication bias was assessed, but was difficult to judge given the small number of studies in each funnel plot. Studies were selected by two reviewers independently to reduce the risk of error; it was not reported whether data extraction and quality assessment were performed in the same way. Study quality was assessed, but the results were poorly reported and this made the quality of the evidence difficult to judge. The method used to pool the studies seemed appropriate, although heterogeneity was high and so pooling may have been inappropriate. Subgroup analyses were used to explore possible reasons for the heterogeneity.

The authors conclusions should be treated with caution given the lack of detail about some review methods and a high level of heterogeneity between the included studies.

**Implications of the review for practice and research**

**Practice:** The authors stated that rapid virological response was an important parameter in determining the success of shorter therapy and shorter treatment durations were less expensive, may reduce side-effects and improve patient compliance. Patients who did not achieve rapid virological response should receive at least 24 weeks pegylated interferon and ribavirin treatment.

**Research:** The authors did not state any implications for research.

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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.