Treatment with peginterferon plus ribavirin vs interferon plus ribavirin for 48 weeks in Chinese patients with chronic hepatitis C
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CRD summary
This review found that Chinese patients with chronic hepatitis C were more likely to achieve a sustained virological response with pegylated interferon plus ribavirin treatment than with interferon plus ribavirin treatment. A lack of reporting of trial quality, small sample sizes, and significant heterogeneity suggest that the reliability of these conclusions is unclear.

Authors' objectives
To compare 48 weeks of pegylated interferon plus ribavirin treatment against interferon plus ribavirin treatment in Chinese patients with chronic hepatitis C.

Searching
MEDLINE and CNKI were searched for studies from 1966 to 2008 published in English or Chinese and the search terms were reported.

Study selection
Randomised controlled trials (RCTs) that compared pegylated interferon against interferon in patients treated for 48 weeks and followed up for 24 weeks were eligible for inclusion if they measured the sustained virological response, which was defined as no detectable hepatitis C virus at six months after treatment finished.

In the included trials, all patients were of Chinese origin, most of them were male and of genotype one, where reported, and the mean age ranged from 34 to 48 years. Pegylated interferon alpha-2a and pegylated interferon alpha-2b were used and the doses and regimens varied between trials.

The authors did not state how many reviewers selected trials for inclusion.

Assessment of study quality
Two reviewers independently assessed trial quality in terms of treatment type, ribavirin dose, follow-up duration, response rate, population, eligibility criteria and participation rate, reasons for dropouts, covariates and confounders, funding, and statistical methods.

Data extraction
Relative risks were extracted by two reviewers and disagreements resolved by discussion. If the patients did not achieve the selected end points they were considered to have failed therapy. Analyses were performed according to intention-to-treat methods.

Methods of synthesis
Relative risks and 95% confidence intervals were pooled in a random-effects meta-analysis, using intention-to-treat methods. Heterogeneity was assessed using $\chi^2$ and I$^2$ statistics. Publication bias was assessed using a funnel plot.

Results of the review
Seven RCTs were included, with 398 patients (range 9 to 48).

Pegylated interferon plus ribavirin was associated with greater sustained virological response than interferon plus ribavirin (RR 1.76, 95% CI 1.21 to 2.56; seven RCTs), but was also associated with significant heterogeneity (p<0.003, I$^2$ 70.3%). Pegylated interferon alpha-2a was associated with significantly higher sustained virological response than interferon alpha-2a (RR 2.26, 95% CI 1.56 to 3.26; four RCTs), but there was no significant difference between pegylated interferon and interferon in the alpha-2b subgroups. No significant heterogeneity was detected. There was no
significant difference between treatments in withdrawals, adverse events, and intercurrent illnesses.

The funnel plot suggested that publication bias might have been present.

**Authors' conclusions**
Chinese patients with chronic hepatitis C had a greater likelihood of achieving a sustained virological response with pegylated interferon plus ribavirin than with interferon plus ribavirin.

**CRD commentary**
The review question was supported by clear inclusion criteria. Only trials published in English or Chinese were sought, which means that publication and language bias cannot be ruled out, and publication bias was suggested by the funnel plot. Validity was assessed, but the criteria used were unclear and it appeared that important ones for the assessment of RCTs were not considered. The results of this assessment were also not reported. The validity assessment and data extraction were performed in duplicate, which reduces the possibility of reviewer error and bias, but similar steps were not reported for trial selection. Significant heterogeneity was detected for the main outcome and, as this was not investigated further, the reliability of the meta-analysis is unclear.

A lack of reporting of trial quality, small sample sizes, and significant heterogeneity in outcomes suggest that the reliability of the authors' conclusions is unclear.

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

**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that, to address the differences in sustained virological response between different ethnic groups, larger RCTs and detailed genotype-specific analyses were needed. The pathogenic mechanism of the hepatitis C virus should also be studied to explain the differences in response rates between different ethnic groups.

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