Interferon therapy in chronic hepatitis B reduces progression to cirrhosis and hepatocellular carcinoma: a meta-analysis

Yang YF, Zhao W, Zhong YD, Xia HM, Shen L, Zhang N

CRD summary
The authors concluded that interferon prevented or delayed the development of liver cirrhosis and hepatocellular carcinoma in patients with chronic hepatitis B. These conclusions should be interpreted with caution as most of the included studies were small and of unknown quality.

Authors’ objectives
To determine whether interferon reduces the incidence of liver cirrhosis and hepatocellular carcinoma in patients with chronic hepatitis B.

Searching
PUBMED and EMBASE were searched from 1986 to May 2008. Search terms were reported. Reference lists of relevant reviews, primary studies, and conference proceedings from major meetings were screened. The review was restricted to studies published as full-text papers or meeting abstracts.

Study selection
Randomised controlled trials (RCTs) and non randomised controlled trials that compared interferon with no treatment in patients with chronic hepatitis B (for more than three years) were eligible for inclusion. Eligible trials had to report sufficient detail on treatment schedule, follow-up and data on liver cirrhosis or hepatocellular carcinoma. Liver cirrhosis was diagnosed by histology or imaging together with the presence of thrombocytopenia, oesophageal varices, ascites or encephalopathy. Hepatocellular carcinoma was diagnosed histologically or by imaging methods, when the alpha-foetoprotein level was above 400ng/ml.

In included studies, interferon doses ranged from 2.5 to 10 million units for six to 52 weeks. Participants mean age ranged from 32 to 57 years; the proportion of women ranged from 6 to 47%. In some studies, all patients had pre-existing cirrhosis. Included studies were conducted in Europe, Japan, Taiwan and Thailand.

The authors did not state how studies were selected for inclusion.

Assessment of study quality
The authors did not state that they assessed study quality.

Data extraction
Two reviewers independently extracted data as relative risks (RR) together with 95% confidence intervals (CI) on an intention-to-treat basis. Disagreements were resolved through discussion.

Methods of synthesis
Summary relative risks were estimated using fixed-effect models in the absence of statistical heterogeneity. Heterogeneity was assessed using the $X^2$ test. Publication bias was assessed using funnel plots and the Egger test.

Results of the review
Eleven studies (n=2,082 patients) were included in the review: one RCT, two case-control studies (although these did not appear to be traditional case-control studies) and eight cohort studies. Duration of follow-up ranged from four to seven years. Alanine transaminase levels were significantly higher in the interferon treated group in three of the studies.

The risk of liver cirrhosis (RR 0.65, 95% CI 0.47 to 0.91; five studies) and hepatocellular carcinoma (RR 0.59, 95% CI 0.43 to 0.81; 11 studies) was significantly lower in patients treated with interferon compared with no treatment. There was no evidence of heterogeneity (p>0.40).
Restriction of the analysis to studies in which alanine transaminase levels were similar at baseline did not alter the findings.

There was no evidence of publication bias (p>0.01).

Authors' conclusions
Interferon prevented or delayed the development of liver cirrhosis and hepatocellular carcinoma in patients with chronic hepatitis B.

CRD commentary
The review addressed a focused question and inclusion criteria were clearly defined. The literature search was adequate for published studies, but restriction of the review to published studies raised the possibility of publication bias; this was assessed in the review and found to be absent. Appropriate steps were taken to minimise bias and errors in data extraction, but it was unclear whether such steps were also taken in the selection of studies.

Study quality was not formally assessed, and the only quality-related factor considered was the baseline comparability of groups. Only one of the included studies was an RCT; the results of this study were not given greater prominence in the review than other studies that used less robust designs. Methods used to pool studies were appropriate. The results were clearly presented using forest plots.

The authors' conclusions are supported by the results, but should be interpreted with caution as most of the included studies were small and of unknown quality.

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