Is antiviral treatment (IFN alpha and/or ribavirin) justified in cirrhosis related to hepatitis C virus?

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Authors' objectives
To assess the efficacy of interferon in patients with post hepatitis C cirrhosis by updating a previous meta-analysis (see Other Publications of Related Interest no.1).

Searching
The search strategy used for the original review was as follows: MEDLINE (dates not stated) using the following search terms: 'chronic hepatitis non-A, non-B, non-C clinical trials', and Current Contents - Clinical Medicine (1985-December 1995). Manual searches of general reviews were carried out and references from published studies were examined. Letters were sent to pharmacological companies.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) in which one intervention arm comprised a fixed dose of interferon. Only published studies were included.

Specific interventions included in the review
3 MU interferon, 3 times per week for 6 months ('standard regimen') and at higher doses.

Participants included in the review
Patients with post hepatitis C cirrhosis.

Outcomes assessed in the review
Alanine transaminase (ALT) response at the end of treatment and sustained ALT response in the months after treatment.

How were decisions on the relevance of primary studies made?
Two independent researchers assessed each study, and conferred in cases of disagreement.

Assessment of study quality
Methodological quality was assessed using "a previously validated questionnaire" (see Other Publications of Related Interest no.2). Two researchers independently applied a questionnaire about methodological quality.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the authors performed the data extraction.

Methods of synthesis
How were the studies combined?
The combined risk differences for change in ALT after treatment and sustained ALT response in the months after treatment were calculated cumulatively using the random-effects model of DerSimonian and Laird (see Other Publications of Related Interest no.3).

How were differences between studies investigated?
The results of tests of heterogeneity were not reported. A sensitivity analysis was conducted including only trials.
recruiting patients with cirrhosis.

Results of the review
Nineteen RCTs (number of participants not stated) were included.

The cumulative meta-analysis ranked in the order of cirrhosis prevalence (range 0% to 100%) showed a decrease in the efficacy of interferon on sustained ALT normalisation but not on the ALT response at the end of the treatment. However, there was always an overall significant effect of interferon versus control, with 43% and 24% of increase response respectively versus controls. When the analysis was repeated with RCTs including only patients with cirrhosis there was a 20% ALT response at the end of interferon treatment versus 0% in the control group (p<0.001), and 13% ALT sustained response versus 0% in the control group (p=0.008).

Authors' conclusions
This overview demonstrates a benefit-risk ratio in favour of interferon in patients with post hepatitis C cirrhosis.

CRD commentary
This review is badly reported, so it is difficult to determine whether it is of good quality. The inclusion criteria and details of the search strategy and review process have been taken from the earlier review. It is unclear whether the search strategy was designed to identify trials of patients with post hepatitis C cirrhosis. No details of study validity are reported, and little information on the individual RCTs is provided. The methods used for combining data from trials is appropriate but heterogeneity is not reported. It is difficult to determine whether the authors' conclusions are justified given that so little information on methods and included trials is given.

It should be noted that several other areas were reviewed in this paper, covering mortality data, efficacy of ribavirin in patients with post hepatitis C cirrhosis, and a meta-analysis of interferon RCTs and non-randomised controlled studies including exclusively patients with post hepatitis C cirrhosis reporting data on morbidity and mortality. However, since there was no report of systematic methods to select, assess, and summarise studies in these categories, these data have not been relayed in this abstract.

Implications of the review for practice and research
Practice: The authors state 'We think that it is mandatory to treat (with interferon) these patients (with post hepatitis C), as the tolerance is roughly similar to that in non-cirrhotic patients. Because of these results, because of an acceptable tolerance and because these patients are at very high risk of death from hepatitis C, we do think that all patients with compensated post hepatitis C cirrhosis PCR positive should be treated for one year'.

Research: The authors state that new RCTs should evaluate the combination of ribavirin-interferon in patients with cirrhosis.

Bibliographic details

PubMedID
9923094

Other publications of related interest
Indexing Status
Subject indexing assigned by NLM

MeSH
Antiviral Agents /therapeutic use; Belgium; Controlled Clinical Trials as Topic; Drug Therapy, Combination; Female; Hepatitis C, Chronic /complications /drug therapy; Humans; Interferons /therapeutic use; Liver Cirrhosis /drug therapy /mortality /virology; Male; Meta-Analysis as Topic; Practice Guidelines as Topic; Randomized Controlled Trials as Topic; Ribavirin /therapeutic use; Survival Analysis; Treatment Outcome

AccessionNumber
11999000452

Date bibliographic record published
31/01/2001

Date abstract record published
31/01/2001

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.