CRD summary
This review assessed the evidence for excluding substance abusers with chronic hepatitis C from treatment with interferon and ribavirin. The authors concluded that there is no evidence to support withholding anti-hepatic C virus treatment, but further research is required. The review presented evidence from poor-quality studies, so any conclusions about treatment effects are suggestive rather than definitive.

Authors' objectives
To assess the evidence for excluding patients with chronic hepatitis C who were substance abusers from treatment with interferon (IFN) and ribavirin.

Searching
Internet guideline clearing houses, MEDLINE, PubMed, the Cochrane Library and DARE were searched for studies conducted between 2001 and 2004; the search terms were reported.

Study selection
Study designs of evaluations included in the review
Clinical trials were eligible for inclusion.

Specific interventions included in the review
Studies of treatments for hepatitis C were eligible for inclusion. The included studies used treatments that changed over the years: from IFN monotherapy, to IFN plus ribavirin and peg-IFN plus ribavirin.

Participants included in the review
Studies of patients with substance abuse and chronic hepatitis C were eligible for inclusion. All of the included studies were conducted in participants with hepatic C caused by intravenous drug use (IVDU). Studies were on former drug users and active users who were or were not taking substitution treatment. The control groups, where present, largely consisted of patients without a history of IVDU. The most frequently abused drugs were heroin and cocaine.

Outcomes assessed in the review
Inclusion criteria for the outcomes were not specified. The review assessed compliance, sustained viral response (SVR), reinfection, adherence to treatment and adverse effects.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

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

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. Data on the outcomes were extracted for each study, where reported.

Methods of synthesis
How were the studies combined?
A narrative synthesis of the studies was undertaken.

How were differences between studies investigated?
Differences could be observed through tabulation of the results.

Results of the review
Ten studies (n=1,208) were included: three open controlled prospective studies (n=554), two open controlled retrospective studies (n=338), one controlled study (n=116), one prospective study (n=50), two open uncontrolled studies (n=100) and one retrospective study (n=50). No randomised controlled trials were included.

There was no reduction in compliance with active substance abuse (three controlled trials). About one third of patients were lost to follow-up in the first 8 weeks of treatment. Active substance abusers not taking substitution therapy were more likely to be lost to follow-up.

The percentage of substance users with a SVR varied from 24 to 48%. There was no difference in SVR between former drug users, active drug users and patients taking substitution treatment compared with control groups. There was no difference between abusers and control groups in SVR (five controlled studies). Patients taking substitution treatment had similar SVR rates to control patients, but active substance abusers not on substitution treatment had significantly lower rates of SVR than patients taking substitution treatment.

The reinfection rates for active IVDU were low: the three studies reported rates of 0% at 24 weeks, 3% after a median of 64 months, and 7%, respectively.

The most common adverse effects with antiviral treatment were fatigue, lack of psychic energy and inertia, weight loss, flu-like syndrome after first injection, nausea and depression. There was no difference in adverse effects between IVDU and non-users (1 study). Rates of discontinuation of treatment varied: 10 to 27% in four studies and 50% in one study of methadone maintenance treatment.

Authors' conclusions
There was no evidence to support withholding anti-hepatic C virus treatment from substance abusers, but further research is required.

CRD commentary
The review question was clear in terms of the participants and interventions, was broadly defined for study design, but was not defined in terms of the outcomes. Several relevant sources were searched but no attempts were made to locate unpublished studies, thus raising the possibility of publication bias. In addition, it was unclear whether any language limitations had been applied. The methods used to select studies and extract the data were not described, so it is not known whether any efforts were made to reduce errors and bias. Validity was not assessed and the methodological limitations of the evidence were not discussed.

Adequate details of the patients' characteristics were tabulated. Given the differences among studies, a narrative summary was appropriate. However, in the summary, studies not listed in the review's tables were referenced and the source of the results reported was often unclear. A more structured narrative synthesis would have been helpful. It was difficult to assess the reliability of the authors' conclusions given the lack of reporting of the review methods and the problems highlighted already. The review presented evidence from poor-quality studies, so any conclusions are suggestive rather than definitive.

Implications of the review for practice and research
Practice: The authors stated that it is important to warn patients about the risks of hepatitis C infection associated with drug use, the risks of coinfection with other viruses, the additive effects of alcohol and drug intake, and the risks of reinfection by needle sharing. They stated that patients should be encouraged to reduce injection drug use and referred to start substitution therapy. They also advised that the patients' social situation be stabilised before IFN treatment is
started, and that multidisciplinary teams should make decisions about antiviral treatment based on an assessment of the individual's risk-benefit.

Research: The authors stated that additional prospective controlled trials on the effects of hepatitis C treatment in active and difficult to reach substance users are required.

Bibliographic details

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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.