An analysis of published trials of interferon monotherapy in children with chronic hepatitis C

Jacobson K R, Murray K, Zellos A, Schwarz K B

Authors' objectives
To determine the efficacy and safety of interferon (IFN) monotherapy in children with chronic hepatitis C (CHC) infection, and to determine predictors of response.

Searching
MEDLINE was searched from January 1990 to November 2000 using 'children', 'hepatitis C' and 'interferon' as the keywords. Conference proceedings and relevant journals were handsearched. Only English language papers were considered.

Study selection
Study design was not a pre-specified inclusion criteria for this review. Studies with or without a comparator (control) were included in the review.

Specific interventions included in the review
Courses of IFN-alpha monotherapy of at least 1.75 MU/m2 at least three times weekly, for at least 6 months, were eligible. The duration of treatment was 6 months or 12 months. In most studies the dose of IFN-alpha was 3 MU/m2 at least three times weekly, whilst in the remaining trials a higher dosage was used. Where there was a comparator it was no treatment. Studies where children were receiving concurrent treatment for leukaemia were excluded.

Participants included in the review
Children aged 21 years or younger with CHC infection, with positive serologies for HCV RNA and negative serologies for human immunodeficiency virus and hepatitis B. In addition, the children were not to have received prior treatment with IFN-alpha and were not to be immunosuppressed. The age range covered in the identified studies was 2 to 21 years.

Outcomes assessed in the review
End-of-treatment response rates and sustained response rates were assessed. Only studies that reported sustained response at 6 months or more were eligible.

How were decisions on the relevance of primary studies made?
One reviewer selected the studies for inclusion according to the inclusion criteria.

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

Data extraction
The authors stated that the data were extracted according to an 'intention-to-treat' strategy, but they do not report how many of the reviewers performed the data extraction.

Methods of synthesis
How were the studies combined?
The sustained response rates were pooled across comparable studies (in terms of study design). The end-of-treatment
response rates and adverse effects were also analysed.

How were differences between studies investigated?
Sustained response rates, stratified by various types of IFN-alpha, were analysed by analysis of variance. The sustained response rates for 6 versus 12 months' treatment, and for a 3 or 1.75 MU/m2 dose three times weekly versus a higher dose (unspecified), were compared using a two-tailed unpaired Student's t-test. The sustained response rates according to genotype were compared using chi-squared. In addition, differences between the studies were described and discussed in the text.

Results of the review
Nineteen studies were identified: four included an untreated control group, the rest were uncontrolled. The total number of treated patients was 366 and 105 were untreated. The number of patients in each study ranged from 5 to 105.

There were no differences in the sustained response rates for various types of IFN-alpha or duration of treatment or dosage. Across the 19 studies, the end-of-treatment response was 54% (range: 0 to 91) and the sustained response was 36% (range: 0 to 73). A spontaneous response rate of 6% occurred in untreated patients. In the four studies where HCV genotype was reported (n=91), the children were classified as genotype 1 or nongenotype 1. Of the 71 children with genotype 1, 27% had a sustained response compared with 70% of the 20 children who were nongenotype 1.

Authors' conclusions
To date there has been no published large-scale, multicentre, prospective placebo-controlled randomised trial of IFN-alpha in children with CHC. The data identified for this review indicate that IFN-alpha in children with CHC is reasonably safe and efficacious.

CRD commentary
This review addressed an appropriate question and the inclusion criteria for the review were adequate. All study designs were included due to a dearth of good-quality trials. The literature search was limited and relevant studies may well have been missed. The details of the primary studies given in the review were very limited. As the studies included were all of a very poor quality, further assessment of quality would have been superfluous. The pooling of the data was simplistic and, therefore, the results of the review should be taken only as an indicator of the possible efficacy of IFN-alpha. Much more research is needed.

Implications of the review for practice and research
Practice: The authors state that the data in this review suggest that IFN-alpha in children with CHC does have reasonable efficacy and safety.

Research: The authors state that this review highlights the need for a more systematic design of future paediatric CHC trials.

Funding
University of Texas, grant number #U19 A140035.

Bibliographic details

PubMedID
11753165
Original Paper URL
http://www.jpgrn.org

Indexing Status
Subject indexing assigned by NLM

MeSH
Adolescent; Adult; Antiviral Agents /adverse effects /therapeutic use; Child; Child, Preschool; Female; Genotype; Hepacivirus /genetics; Hepatitis C, Chronic /drug therapy; Humans; Interferon-alpha /adverse effects /therapeutic use; MEDLINE; Male; Polymerase Chain Reaction; RNA, Viral /analysis; Recurrence; Safety; Treatment Outcome

AccessionNumber
12002000111

Date bibliographic record published
30/11/2003

Date abstract record published
30/11/2003

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.