

Review: Interferon- α plus ribavirin improves the virologic response in chronic hepatitis C

Kjaergard LL, Krogsgaard K, Gluud C. Interferon alfa with or without ribavirin for chronic hepatitis C: systematic review of randomised trials. *BMJ*. 2001 Nov 17;323:1151-5.

QUESTION

In patients with chronic hepatitis C, is interferon- α plus ribavirin more effective than interferon- α alone for improving hepatitis C virologic response and liver-related morbidity and mortality?

DATA SOURCES

Studies were identified by searching the controlled trials register of the Cochrane Hepato-Biliary Group, the Cochrane Library, EMBASE/Excerpta Medica, and MEDLINE (all to August 2000) and by hand searching specialist journals. Bibliographies of relevant articles were reviewed, and authors of included trials and pharmaceutical companies were contacted for unpublished studies.

STUDY SELECTION

Studies in any language were selected if they were randomized controlled trials comparing interferon- α plus ribavirin (combination group) with interferon- α alone in patients with chronic hepatitis C. Patients were either interferon-naïve (not previously treated with interferon), relapsers (patients with a transient biochemical or virologic response to previous interferon therapy), or nonresponders (patients who did not respond to previous interferon therapy). Studies of patients

with hepatitis B, HIV infection, or hepatic decompensation were excluded.

DATA EXTRACTION

Data were extracted on study design, patient characteristics, details of the intervention, study duration, study quality, and outcomes. The primary outcome measures were virologic response (loss of detectable hepatitis C virus RNA) at the end of the treatment, 6 months after treatment, and > 6 months after treatment; liver-related morbidity (cirrhosis, hepatocellular carcinoma, and liver transplantation); and mortality.

MAIN RESULTS

48 trials (6585 patients) met the selection criteria. Meta-analyses were done by using random-effects models. More patients in the interferon group than in the combination group did not have a virologic response at

the end of treatment (relative risk [RR] for naïve patients 0.72, 95% CI 0.65 to 0.79; for relapsers 0.53, CI 0.38 to 0.74; and for nonresponders 0.83, CI 0.79 to 0.88), at 6 months after treatment (Table), and at > 6 months after treatment (RR for all patients 0.75, CI 0.62 to 0.91). The groups did not differ for liver-related morbidity and all-cause mortality.

CONCLUSION

In patients with chronic hepatitis C, interferon- α plus ribavirin is more effective than interferon- α alone for improving the hepatitis C virologic response, but not for reducing liver-related morbidity and mortality.

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Interferon- α plus ribavirin (IAPR) vs interferon- α (IA) for chronic hepatitis C*

No virologic response at 6 mo	Weighted event rates		RRR (95% CI)	NNT (CI)
	IAPR	IA		
Naïve patients	64%	87%	26% (22 to 30)	5 (4 to 6)
Relapsers	61%	90%	33% (22 to 43)	4 (2 to 6)
Nonresponders	88%	98%	9% (3 to 15)	11 (7 to 30)

*Abbreviations defined in Glossary; weighted event rates, RRR, NNT, and CI calculated from data provided by the author using random-effects models.

COMMENTARY

The review by Kjærgard and colleagues shows that for patients with chronic hepatitis C, the combination of interferon- α and ribavirin is superior to interferon- α alone in interferon-naïve patients, relapsers, and nonresponders. A wide range of dosages for both interferon- α and ribavirin was used in these trials, and despite 20 years of experience with interferon- α , the optimal dosage remains unknown.

Neither interferon- α plus ribavirin nor interferon- α alone decreased hepatic morbidity or mortality in this review. This is not surprising because the post-treatment follow-up was only 6 months in most trials. In patients with compensated cirrhosis, morbidity and mortality are reduced (1).

Genotype was not considered in this meta-analysis, but response rates vary from about 20% in genotype 1 to 65% in genotype 3 (2). Conventional interferon will soon be replaced by the more efficacious pegylated interferons (3). When combined with ribavirin, they achieve sustained response rates of about 45% in genotype 1 and about 80% in genotype 3 (4). Taking into account that only 4% of patients die of hepatitis C (5) and that better treatments are on the horizon, only a

small number of patients need to be treated with the essentially obsolete regimens assessed in this review.

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