Pegylated interferon monotherapy of chronic hepatitis C in dialysis patients: meta-analysis of clinical trials

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CRD summary
The review concluded that pegylated interferon did not provide an added benefit in terms of virological response compared with standard interferon monotherapy. Tolerance to pegylated interferon monotherapy was unsatisfactory. The authors’ conclusions were based on data of unknown quality and must be interpreted with caution.

Authors’ objectives
To collate the evidence on the tolerability and efficacy of initial monotherapy with pegylated interferon in chronic renal failure patients with chronic hepatitis C.

Searching
MEDLINE was searched from 1995 to July 2008 for published articles in any language. Search terms were reported. Manual searches were conducted of general reviews, references from published clinical trials, letters to pharmacological companies and Current Contents.

Study selection
Published studies of primary monotherapy with pegylated interferon that reported sustained virological response as a clinical endpoint in dialysis patients with chronic hepatitis were eligible for inclusion. Secondary end points were tolerability measured by drop-out rate, end of treatment virological and biochemical response and sustained biochemical response. Studies were excluded if they included patients with coexisting diseases such as infection with HIV (human immunodeficiency virus), haemophilia or other aetiology of liver disease such as hepatitis B or A, or Epstein-Barr virus. Studies that included previously treated patients, non-responders or relapsed patients were excluded. Studies that reported viral response rates via methods other than polymerase chain reaction were excluded, as were studies that included patients with functioning renal grafts. Abstracts and interim reports were ineligible.

The included studies evaluated pegylated interferon alpha-2a (dose ranged from 1.5mcg/kg to 180mcg every week) or pegylated interferon alpha-2b (dose ranged from 0.5 to 135mcg/kg/week) over 24 to 48 weeks. Patient ages ranged from 35 to 57 years. The proportion of men varied from 40% to 100%. Studies mostly included patients with primarily genotype 1; some genotype 2 to 3 patients were included.

The authors did not state how many reviewers were involved in study selection. But they stated that there was 100% concordance between reviewers concerning inclusion criteria, which indicated that at least two reviewers were involved in the process.

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

Data extraction
Two authors independently extracted data on sustained virological response and drop-out rates and calculated pooled response rates and 95% confidence intervals (CIs). Data were analysed on an intention-to-treat basis. Response rates were calculated if they were not provided by study authors.

Methods of synthesis
Pooled response rates and drop-out rates, together with 95% CIs, were calculated using a random-effects meta-analysis. Statistical heterogeneity was assessed using X^2 and I^2 statistics. Subgroup analysis grouped studies according to type of pegylated interferon, type of study and location of study. Sensitivity analysis was conducted using fixed-effects meta-analysis for publication year, age, sex, time on dialysis, genotype, biochemical response, virological response, discontinuation, pegylated interferon dose and duration.
Results of the review
Sixteen studies (n=254 patients) were included in the review: two randomised controlled trials; three controlled trials; and 11 cohort studies. Sample sizes ranged from three to 78 patients.

Sustained virological response rate for all studies was 0.33 (95% CI 0.24 to 0.43, $I^2=57\%$; 15 studies). Summary dropout rate was 23% (95% CI 14 to 33, $I^2=79\%$; number of studies unknown). The most frequently reported side-effects that interrupted treatment were haematological abnormalities (18%), gastrointestinal (14%), neurological (10%) and cardiovascular (10%). Influenza-type symptoms were common, but did not frequently lead to withdrawal.

Subgroup analysis resulted in sustained virological response rates that ranged from 0.20 (95% CI 0.08 to 0.32, $I^2=15\%$; four studies) for pegylated interferon alpha-2b patients to 0.25 (95% CI 0.19 to 0.31, $I^2=61\%$; 10 studies) for pegylated interferon alpha-2a patients. The highest sustained virological response rates were observed in controlled studies (sustained virological response 0.38, 95% CI 0.18 to 0.59, $I^2=66\%$; five studies). The summary drop out rate for the controlled studies was 15% (95% CI 3 to 26, $I^2=67\%$; five studies). Sensitivity analysis revealed an association between sustained virological response and publication year, time on dialysis, end-of treatment virological response and end-of treatment biological response.

Authors’ conclusions
Pegylated interferon did not provide an added benefit in terms of virological response compared with standard interferon monotherapy. Tolerance to pegylated interferon monotherapy was unsatisfactory.

CRD commentary
Inclusion criteria for the review were clearly defined. One relevant database was searched and some manual searching was undertaken. Publication bias was not assessed and could not be ruled out. Two reviewers appeared to undertake study selection and data extraction, which should have minimised risks of error and bias in the analysis. The authors did not report whether quality assessment was undertaken, which made quality assessment of the included studies difficult. The studies were combined using meta-analysis and subgroup and sensitivity analysis were undertaken, which appeared appropriate. However, the small number of included trials of low-quality study design and small sample size, together with the lack of quality assessment, limits the reliability of the authors’ conclusions.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that further studies were in progress to assess the optimal antiviral therapy for chronic hepatitis C in dialysis patients.

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