Effect of lipid reduction on the progression of renal disease: a meta-analysis

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Authors' objectives
To examine the effects of antilipemic agents on the glomerular filtration rate (GFR) and proteinuria or albuminuria, in patients with renal disease.

Searching
MEDLINE was searched to July 1, 1999 using the keywords 'hyperlipidemia', 'cholesterol', 'diabetes' and 'nephrotic syndrome'. The bibliographies of retrieved and other recent articles were reviewed to locate additional studies. Abstracts from major nephrology meetings over the previous 10 years, including the American Society of Nephrology and the International Congress of Nephrology, were also searched. Only studies that were published as full reports in peer-reviewed journals or as abstracts were included.

Study selection
Study designs of evaluations included in the review
Prospective controlled studies with a parallel or crossover design control group. Uncontrolled and historical control studies were excluded, as were studies that treated participants for less than 3 months. The specific study designs included in the review were randomised controlled trials (RCTs), randomised crossover trials, and a controlled trial in which the patients were alternately allocated to the treatment and control groups.

Specific interventions included in the review
Antilipemic agents. The specific treatments included in the review were simvastatin, pravastatin, lovastatin, gemfibrozil, probucol and fluvastatin.

Studies were excluded if they only examined the effects of diet or dietary supplements on renal function or proteinuria. In particular, studies examining the effects of fish oil or other dietary fatty acid supplements were excluded.

Participants included in the review
Patients with renal disease. The disease status of the participants included diabetes and glomerulonephritis. The proportion of male patients ranged from 25 to 80% (mean 61%). The mean age of the patients ranged from 36 to 65 years (the mean of the study means was 49 years).

Outcomes assessed in the review
GFR and proteinuria or albuminuria. The primary outcome of interest was a change in the estimated GFR. The secondary outcome of interest was a change in proteinuria or urine albumin excretion.

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

Assessment of study quality
The validity of the primary studies was assessed according to a study quality index defined by the authors. The criteria used were random allocation of the patients, use of parallel group design, use of crossover design, clear delineation of inclusion and exclusion criteria, masking of the patients, and masking of the investigators. Two authors independently extracted the data on study quality, and any differences were resolved by conferencing.

Data extraction
Two authors independently extracted the data, and any differences were resolved by conferencing.
The categories of data extracted included: author and year of study; study design; the number and age of participants; the gender of participants; study duration; cause of renal disease, i.e. diabetes, glomerulonephritis, or other/unknown; treatment; the end point studied, i.e. GFR or proteinuria; the baseline GFR and cholesterol level in the treatment and control groups; and the change in serum cholesterol and blood-pressure in the treatment and control groups.

Methods of synthesis
How were the studies combined?
Weighted means and confidence intervals (CIs) were calculated for the combined differences between the treatment and control groups using a fixed-effect model. The results of the trials were also combined using a random-effects model, as described by DerSimonian and Laird (see Other Publications of Related Interest no.1). Publication bias was assessed using a funnel plot.

How were differences between studies investigated?
Differences between studies were investigated using the chi-squared test for heterogeneity. Heterogeneity between trials was also investigated using a L’Abbe plot (see Other Publications of Related Interest no.2).

Results of the review
Thirteen studies (n=404) met the inclusion criteria: 10 RCTs (n=347), 2 randomised crossover trials (n=40), and 1 controlled trial (n=17) in which participants were alternately allocated to the treatment and control groups.

GFR (12 studies): 94% (362 of 384) of the patients completed the follow-up. Using the fixed-effect model, the mean weighted effect of lipid-lowering treatment on the change in GFR was 0.156 mL/minute per month (95% CI: 0.026, 0.285, p=0.008). This indicated that treatment with lipid-reducing agents had a favourable effect on GFR. The combined treatment effect and CIs were the same for the random-effects model. In addition, removing the trial that was not truly random had no effect on the result: the effect of treatment remained at 0.156 mL/minute per month (95% CI: 0.025, 0.289, p=0.008).

A chi-squared test for heterogeneity between the studies was not statistically significant. A L’Abbe plot failed to reveal any marked heterogeneity between the trials.

A funnel plot failed to suggest that there was publication bias.

The regression analysis showed no correlation between the effects of treatment on GFR and study quality, the percentage change in cholesterol, the type of lipid-lowering agent, or the cause of renal disease. However, there was a correlation shown between longer follow-up and the effect of treatment on GFR improvement (p=0.007).

Proteinuria (11 studies): 94% (246 of 262) of the patients completed the follow-up. Using the fixed-effect model, the mean weighted effect of treatment on the change in urine protein or albumin excretion was -0.283 (95% CI: -0.427, -0.139, p<0.001). The results were not statistically significant when using the random-effects method: the mean weighted mean was -0.249 (95% CI: -0.562, +0.064, p=0.077).

A chi-squared test for heterogeneity between the studies was statistically significant (p<0.001), thus questioning the validity of combining the results. A subsequent regression analysis to investigate the differences between study results found no obvious explanation for this heterogeneity.

A funnel plot failed to suggest that there was publication bias.

Quality assessment.

Of the included trials, 10 were randomised and controlled, 1 assigned every other patient to the treatment or control groups, and 2 used a randomised crossover design. The masking of the investigators and participants varied across the trials: both the investigators and the participants were masked in 6 trials; neither the investigators nor the participants were masked in 4 trials; in 1 trial, the participants but not the investigators were masked; and in 2 trials, the information on masking was unavailable.
Authors' conclusions
Lipid-lowering therapy in patients with renal insufficiency may help slow the rate of renal disease progression. Lipid reduction may also preserve the GFR and decrease proteinuria in patients with renal disease.

CRD commentary
The review question was clearly stated and was well supported by the inclusion criteria.

The literature search was comprehensive, but there was no attempt to identify unpublished research. In addition, the authors did not specify if foreign language publications were eligible for inclusion.

The quality assessment of the primary studies was adequate, and the data were synthesised appropriately. Heterogeneity and publication bias were adequately assessed. Some details regarding the review process were provided, such as how the judgements of validity were made and how the data were extracted from the primary studies. However, other details were not provided, e.g. how the decisions on the relevance of the primary studies were made.

The authors' conclusions follow on from the results.

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

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Other publications of related interest

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