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COCHRANE COMMENTARY

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Statins for end-stage kidney disease treated with dialysis

WHAT IS THIS REVIEW ABOUT?

This systematic review summarized the available evidence for the efficacy and safety of statin therapy in adults with end-stage kidney disease treated with dialysis. The review assessed the efficacy and safety of statin drugs (atorvastatin, cerivastatin, fluvastatin, lovastatin, pitavastatin, pravastatin, rosuvastatin and simvastatin with or without combined ezetimibe therapy) against placebo or another statin. We focus here on the available evidence in placebo-controlled trials for treatment effects on mortality, cardiovascular, adverse event and lipid end-points.

WHAT ARE THE FINDINGS?

Compared with placebo, statin therapy had little or no effect on major cardiovascular events (4 trials, 7084 participants; relative risk (RR) 0.95 (confidence interval (CI) 0.88–1.03)), all-cause mortality (13 studies, 4705 participants; RR 0.96 (CI 0.90–1.02)) cardiovascular death (13 trials, 4627 participants; RR 0.94 (CI 0.84–1.06)) and myocardial infarction (3 trials, 4047 participants; RR 0.87 (CI 0.71–1.07)) and uncertain effects on stroke (2 trials, 4018 participants; RR 1.29 (CI 0.96–1.72)) (Fig. 1).

Statin therapy had uncertain effects on potential adverse events including elevation in creatine kinase (5 trials, 3067 participants; RR 1.25 (CI 0.55–2.83)) and liver function enzymes (4 trials, 3044 participants; RR 1.09 (CI 0.41–1.25)), withdrawal due to adverse events (9 trials, 1832 participants; RR 1.04 (CI 0.87–1.25)) and cancer (2 trials, 4012 participants; RR 0.90 (CI 0.72–1.11)).

Statin treatment lowered serum total cholesterol (14 trials, 1803 participants; mean difference (MD) −1.16 mmol/L (CI −1.43 to −0.89)) and low-density lipoprotein cholesterol (12 trials, 1747 participants; MD −1.04 mmol/L (CI −1.36 to −0.71) levels.

WHAT ARE THE FINDINGS BASED ON?

Twenty-three trials compared statin therapy *versus* placebo in 8166 participants treated with dialysis. Eleven trials involved adults treated with haemodialysis and five studies included only peritoneal dialysis patients. Study sample sizes ranged between 13 and 3023 participants (median 42). Doses of statin were generally equivalent to simvastatin 20 mg daily (range 5 mg to 80 mg) and the median follow-up was 6 months (range 2 to 59 months). Overall, when any limitations in study design, the consistency of results across different trials, the certainty of treatment effects and the chances of missing unpublished results were all considered, there were moderate to high levels of confidence in the available

Outcome	No. of trials (participants)	Relative risk (95% confidence interval)
Major cardiovascular event	4 (7084)	0.95 (0.88 to 1.03)
Cardiovascular mortality	13 (4627)	0.94 (0.84 to 1.06)
All-cause mortality	13 (4705)	0.96 (0.90 to 1.02)
Myocardial infarction	3 (4047)	0.87 (0.71 to 1.07)
Stroke	2 (4018)	1.29 (0.96 to 1.72)
Elevated creatine kinase	5 (3067)	1.25 (0.55 to 2.83)
Deranged liver function	4 (3044)	1.09 (0.41 to 1.25)
Withdrawal from treatment	9 (1832)	1.04 (0.87 to 1.25)
Cancer	2 (4012)	0.90 (0.72 to 1.11)

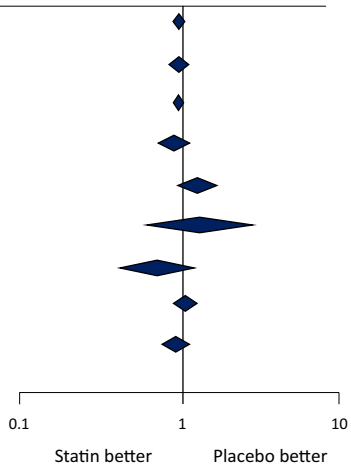

Fig. 1 Effects of statin therapy (all agents) *versus* placebo on clinical outcomes in people who had end-stage kidney disease treated with dialysis.

results. This suggested that additional research was unlikely to change the confidence in these results.

IMPLICATIONS FOR PRACTICE

- In adults with end-stage kidney disease, statin had little or no effect on mortality and major cardiovascular end-points despite clinically relevant reductions in serum cholesterol.
- The available evidence for the efficacy of statin therapy in adults with end-stage kidney disease was high quality, suggesting additional research is unlikely to improve our confidence in the evidence for treatment efficacy.

CLINICAL PERSPECTIVE

Despite high absolute risks of cardiovascular disease and mortality (approaching 20% each year) in adults treated with dialysis, statin therapy has little effect on cardiovascular and mortality risk in this setting. This is in contrast to the 20% to 25% proportional reduction in these outcomes with statin therapy in adults with less severe kidney disease and despite clinically important reductions in serum cholesterol with treatment. It is likely that adults treated with dialysis experience cardiovascular complications as a result of myocardial hypertrophy and fibrosis as well as vascular calcification, which are disease processes that are less modifiable by statin therapy than occlusive atherosclerosis, commonly seen in populations with earlier stages of chronic kidney disease. Overall, statin therapy is not effective in people treated with dialysis and treatment-related harms are uncertain.

Palmer SC, Navaneethan SD, Craig JC *et al*. HMG CoA reductase inhibitors (statins) for dialysis patients. *Cochrane Database of Systematic Reviews* 2013, Issue 9. Art No.: CD004289. DOI: 10.1002/14651858.CD004289.pub5.

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