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COCHRANE COMMENTARY

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Statins for kidney transplant recipients

What is this review about?

This systematic review summarized the available evidence for the efficacy and safety of statin therapy in adult recipients of a kidney transplant. 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?

Statin therapy may possibly reduce major cardiovascular events (1 trial, 2102 participants; relative risk (RR) 0.84 (confidence interval (CI) 0.66–1.06)), cardiovascular death (4 trials, 2322 participants; RR 0.68 (CI 0.45–1.01)) and myocardial infarction (1 trial, 2102 participants; RR 0.70 (CI 0.48–1.01)), although these effects were not statistically significant. Statin treatment had uncertain effects on all-cause mortality (6 trials, 2760 participants; RR 1.08 (CI 0.63–1.83)) and stroke (1 trial, 2102 participants; RR 1.18 (CI 0.85–1.63)) (Fig. 1).

Statin therapy had uncertain effects on potential adverse events including elevation in creatine kinase (3 trials, 2322 participants; RR 0.86 (CI 0.39–1.89)) and liver function enzymes (4 trials, 608 participants; RR 0.62 (CI 0.33–1.19)), withdrawal due to adverse events (9 trials, 2810 participants; RR 0.89 (CI 0.74–1.06)) and cancer (1 trial, 2094 participants; RR 0.94 (CI 0.82–1.07)).

Statin treatment lowered serum total cholesterol (12 trials, 3070 participants; mean difference (MD) −1.10 mmol/L (CI −1.33 to −0.87)) and low-density lipoprotein cholesterol (11 trials, 3004 participants; MD −1.12 mmol/L (CI −1.36 to −0.87) levels.

What are the findings based on?

Seventeen trials compared statin therapy *versus* placebo in 3282 adult recipients of a kidney transplant. The majority of data were derived from the Assessment of LEscol in Renal Transplantation (ALERT) study, which was a large (2102 participants) well-conducted double-blind trial. Study sample sizes were generally small ranging between 20 and 2012 participants (median 48). Doses of statin were generally equivalent to simvastatin 10 mg daily (range 5 mg to 40 mg) and the median follow-up was 4 months (range 2 to 61

Outcome	No. of trials (participants)	Relative risk (95% confidence interval)
Major cardiovascular event	1 (2102)	0.84 (0.66 to 1.06)
Cardiovascular mortality	4 (2322)	0.68 (0.45 to 1.01)
All-cause mortality	6 (2760)	1.08 (0.63 to 1.83)
Myocardial infarction	1 (2102)	0.70 (0.48 to 1.01)
Stroke	1 (2102)	1.18 (0.85 to 1.63)
Elevated creatine kinase	3 (2322)	0.86 (0.39 to 1.89)
Deranged liver function	4 (608)	0.62 (0.33 to 1.19)
Withdrawal from treatment	9 (2810)	0.89 (0.74 to 1.06)
Cancer	1 (2094)	0.94 (0.82 to 1.07)

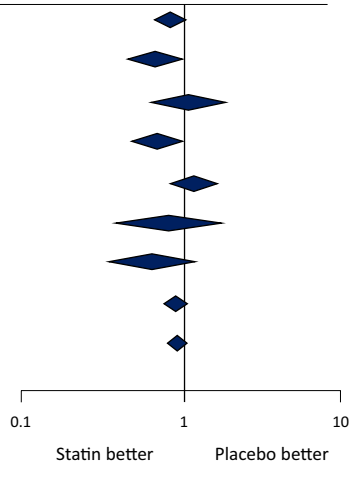

Fig. 1 Effects of statin therapy (all agents) *versus* placebo on clinical outcomes in adult recipients of a kidney transplant.

months). Two studies were conducted in transplant recipients who had no history of cardiovascular disease. 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 low levels of confidence in the available results. This suggested that additional research was likely to have an important impact on the results and was likely to change the estimated effects of treatment.

Implications for practice

- In adult kidney transplant recipients, statin treatment (simvastatin 10 mg daily equivalent) may reduce cardiovascular mortality and major cardiovascular end-points but has uncertain effects on overall mortality risk.
- Evidence for treatment harms of statins in kidney transplant recipients is uncertain.
- The confidence in the evidence for the efficacy and safety of statin therapy in kidney transplant recipients is low, suggesting additional research is needed.

Clinical perspective

Currently, statin therapy may reduce cardiovascular events in kidney transplant recipients although future research is needed to increase the confidence in this result. Statin doses in existing trials are low (simvastatin 10 mg daily equivalent) and the benefits and harms of higher doses are unknown. The lack of information about treatment-related harms in this population precludes robust assessments of the trade-off between efficacy and toxicity of statin treatment in individual patients.

Palmer SC, Navaneethan SD, Craig JC *et al*. HMG CoA reductase inhibitors (statins) for kidney transplant recipients. *Cochrane Database of Systematic Reviews* 2014, Issue 1. Art. No.: CD005019. DOI: 10.1002/14651858.CD005019.pub4.