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Cochrane Database of Systematic Reviews 2013, Issue 12. Art. No.: CD005425.
DOI: 10.1002/14651858.CD005425.pub2.

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[Intervention Review]

Lipid-lowering agents for nephrotic syndrome

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Editorial group: Cochrane Kidney and Transplant Group.
Publication status and date: New, published in Issue 12, 2013.

Citation: Kong X, Yuan H, Fan J, Li Z, Wu T, Jiang L. Lipid-lowering agents for nephrotic syndrome. *Cochrane Database of Systematic Reviews* 2013, Issue 12. Art. No.: CD005425. DOI: 10.1002/14651858.CD005425.pub2.

ABSTRACT

Background

Nephrotic syndrome is the collective name given to a group of symptoms that include proteinuria, lipiduria, hypoalbuminaemia, oedema, hypercholesterolaemia, elevated triglycerides, and hyperlipidaemia. Hyperlipidaemia is thought to aggravate glomerulosclerosis (hardening of blood vessels in the kidneys) and enhance progression of glomerular disease. Studies have established that reduction in total cholesterol and low density lipoprotein (LDL) cholesterol is associated with reduction in risk of cardiovascular diseases. In 2011, the European Society of Cardiology and European Atherosclerosis Society guidelines for the management of dyslipidaemia recommended use of statins as first-line agents in the management of nephrotic dyslipidaemia. However, the effectiveness and safety of statins for people with nephrotic syndrome remains uncertain. Furthermore, the efficacy of second-line lipid-lowering drugs, such as ezetimibe and nicotinic acid, has not been proven in patients with nephrotic syndrome who are unable to tolerate statin therapy.

Objectives

This review aimed to evaluate the benefits and harms of lipid-lowering agents in adults and children with nephrotic syndrome.

Search methods

We searched the Cochrane Renal Group's Specialised Register (to 18 March 2013) through contact with the Trials Search Co-ordinator using search terms relevant to this review.

Selection criteria

All randomised controlled trials (RCTs) and quasi-RCTs (RCTs in which allocation to treatment was obtained by alternation, use of alternate medical records, date of birth or other predictable methods) looking at participants with nephrotic syndrome that compared any lipid-lowering agent to placebo, no treatment or other lipid-lowering agents, given for not less than four weeks, were included.

Data collection and analysis

Two authors independently assessed study eligibility and risk of bias, and extracted data. Statistical analyses were performed using a random effects model. Dichotomous results were expressed as risk ratios (RR) with 95% confidence intervals (CI). For continuous measures mean difference (MD) was used, or the standardised mean difference (SMD) where different scales had been used.

Main results

We included five RCTs enrolling a total of 203 participants. Of these, four studies compared statins with no treatment or placebo, and one compared fibrates with placebo. We found no published studies comparing second-line agents such as ezetimibe, bile acid sequestrants, and nicotinic acid with placebo or no treatment. Our assessment of the risk of bias found that one study was judged overall to be at low risk of bias and the remaining four were judged to be at high risk of bias.

Most outcomes were supported by single study data. One study reported significantly increased high density lipoprotein (HDL) cholesterol among participants in the statin arm compared with the no treatment group (MD 5.40 mg/dL, 95% CI 2.31 to 8.49). Another study reported higher serum albumin in the statin group compared to those who received no treatment (MD 0.60 g/dL, 95% CI 0.14 to 1.06). No serious adverse events, such as rhabdomyolysis, were reported, however some minor events occurred. One study reported no significant difference in the number of participants with elevated liver enzymes (RR 3.00, 95% CI 0.13 to 69.52); three studies reported liver enzymes remained within the normal range (no data provided). Four studies reported creatinine phosphokinase (CPK). One study indicated that CPK values fluctuated in both the simvastatin and placebo groups (no data provided); the remaining three studies reported CPK either stayed within the normal range (one study) or there was no significant difference between the lipid lowering agents and placebo.

Authors' conclusions

None of the included studies reported patient-centred outcomes including all-cause mortality, cardiovascular mortality, or non-fatal myocardial infarction; only single studies reported cholesterol (HDL, LDL and total cholesterol), triglycerides, serum creatinine, blood urea nitrogen, liver enzymes, and protein (serum, urine). High quality RCTs need to be conducted to assess the safety and efficacy of lipid-lowering drugs for people with nephrotic syndrome.

PLAIN LANGUAGE SUMMARY

Lipid-lowering agents for nephrotic syndrome

Nephrotic syndrome is a relatively rare disease in which the kidneys leak protein into the urine. A common early sign is swelling in the feet and face. Other signs and symptoms of nephrotic syndrome include low levels of protein in the blood, and high levels of fats in the blood, particularly cholesterol and triglycerides.

Managing nephrotic syndrome includes therapies to reduce fats (lipids) in the blood. Several types of lipid-lowering agents including statins, bile acid sequestrants, nicotinic acid and ezetimibe can be used.

We looked for evidence from RCTs to establish if lipid-lowering drugs were beneficial for people with nephrotic syndrome. We found five small studies that investigated four different lipid-lowering drugs (simvastatin, lovastatin, fluvastatin, gemfibrozil) in 203 participants with nephrotic syndrome.

There is currently not enough high quality evidence from published studies to determine if lipid-lowering agents are helpful in managing dyslipidaemia in people with nephrotic syndrome.