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High-potency statins are associated with increased hospitalisations with acute kidney injury

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Context

Statins are commonly used medications for the reduction of low-density lipoprotein cholesterol resulting in markedly improved cardiovascular disease outcomes.¹ Prior studies with regard to acute kidney injury (AKI) risk in statin users versus non-statin users show mixed results. Dormuth and colleagues address the question of whether high-potency statin therapy is associated with increased hospitalisation for AKI compared to low-potency statin therapy, thereby decreasing indication bias for statin use as a confounder.

Methods

The Canadian Network for Observational Drug Effect Studies (CNODES) are an observational retrospective database meta-analysis of 2 008 003 patients without chronic kidney disease (CKD) and 59 636 with CKD. Patients were identified from three databases: the General Practice Research Database in the UK, the Caremark-Medicare database in the USA and data on new prescriptions for statins from seven Canadian provinces between 1997 and 2008. The primary outcome was hospitalisation with AKI as identified by the WHO International Classification of Diseases coding. The patients were matched for possible confounders by high-density propensity scoring.

Findings

The primary outcome of adjusted rate ratio (RR) for hospitalisation for AKI was significant (RR=1.34, 95% CI 1.25 to 1.43) in patients on high-potency statin therapy without CKD in the first 120 days after starting therapy. This was decreased after longer duration of treatment; for days 121–365 (RR=1.11, 95% CI 1.04 to 1.19) and for days 366–730 (RR=1.15, 95% CI 1.09 to 1.22). Patients on high-potency statin therapy with CKD had no significant increase in hospitalisation for AKI when compared to low-potency statin therapy at all time periods.

The χ^2 tests for heterogeneity were not significant for all meta-analyses except for past use in patients with CKD.

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Competing interests None.

Commentary

The CNODES study strengthens the evidence that high-potency statins are associated with increased risk of AKI. Large number of patients followed for many years are needed to show statistically significant differences in rare adverse events. The study accomplishes this by using a retrospective database search that results in an inability to randomise. Although propensity score matching was used, it was not possible to control for all confounders. The patients in the high-potency statin group without CKD had a higher use of ACE inhibitors, angiotensin receptor blockers and non-steroidal anti-inflammatory drugs which are associated with increased AKI.

Despite increased hospitalisations with AKI in this study, statins are an attractive choice as renoprotective drugs. In preclinical studies in rodents, statins have been observed to improve AKI.² In humans, pre-operative statin use is associated with a decreased risk of postoperative AKI.³ In a randomised study, patients assigned to atorvastatin 80 mg within 24 h before contrast media exposure had a significantly lower rate of AKI than control patients.⁴

The relationship between high-potency statin exposure and the risk of AKI remains as an association. Future analysis is necessary to see if nephrotoxicity is related to potency or specific statins. Analysis of AKI episodes is needed to classify the underlying cause as acute tubular necrosis, acute interstitial nephritis, rhabdomyolysis, or some other cause of renal injury. Studies of the potential renal side effects of high-potency statin therapy need to be reconciled with studies of the renoprotective effects of statins against AKI.

While the increased risk of AKI is statistically significant, the increased risk of AKI needs to be tempered with the clinical benefits of statin therapy. The analysis of the data shows that treatment of 1700 patients with high-potency statins for 120 days results in one hospitalisation with a diagnostic code for AKI. Analysis of the JUPITER study in patients without CKD and with elevated C reactive protein receiving rosuvastatin 20 mg daily showed a statistically significant decrease in the combined endpoint of myocardial infarction, stroke or death from cardiovascular causes and death from any cause after a median follow-up of 1.9 years.⁵ In the JUPITER study, the number of patients in the rosuvastatin group that had greater than 100% increase in serum creatine from baseline was not statistically different from the placebo group. Thus, the benefits of high-potency statins in reducing cardiovascular disease and mortality seem to outweigh the relatively small risk of AKI.

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