Original Research | 18 June 2013

Statin Toxicity From Macrolide Antibiotic Coprescription: A Population-Based Cohort Study

Amit M. Patel, MD; Salimah Shariff, PhD; David G. Bailey, BScPhm, PhD; David N. Juurlink, MD, PhD; Sonja Gandhi, BSc; Muhammad Mamdani, PharmD, MPH; Tara Gomes, MHSc; Jamie Fleet, BSc; Y. Joseph Hwang, BMSc; and Amit X. Garg, MD, PhD

[+] Article and Author Information

Text Size: A A A

Background: Clarithromycin and erythromycin, but not azithromycin, inhibit cytochrome P450 isoenzyme 3A4 (CYP3A4), and inhibition increases blood concentrations of statins that are metabolized by CYP3A4.

Objective: To measure the frequency of statin toxicity after coprescription of a statin with clarithromycin or erythromycin.


Setting: Ontario, Canada, from 2003 to 2010.

Patients: Continuous statin users older than 65 years who were prescribed clarithromycin (n = 72 591) or erythromycin (n = 3267) compared with those prescribed azithromycin (n = 68 478).

Measurements: The primary outcome was hospitalization with rhabdomyolysis within 30 days of the antibiotic prescription.

Results: Atorvastatin was the most commonly prescribed statin (73%) followed by simvastatin and lovastatin. Compared with azithromycin, coprescription of a statin with clarithromycin or erythromycin was associated with a higher risk for hospitalization with rhabdomyolysis (absolute risk increase, 0.02% [95% CI, 0.01% to 0.03%]; relative risk [RR], 2.17 [CI, 1.04 to 4.53]) or with acute kidney injury (absolute risk increase, 1.26% [CI, 0.58% to 1.95%]; RR, 1.78 [CI, 1.49 to 2.14]) and for all-cause mortality (absolute risk increase, 0.25% [CI, 0.17% to 0.33%]; RR, 1.56 [CI, 1.36 to 1.80]).

Limitations: Only older adults were included in the study. The absolute risk increase for rhabdomyolysis may be underestimated because the codes used to identify it were insensitive.

Conclusion: In older adults, coprescription of clarithromycin or erythromycin with a statin that is metabolized by CYP3A4 increases the risk for statin toxicity.

Primary Funding Source: Academic Medical Organization of Southwestern Ontario.