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DYSLIPIDAEMIA

Risks of statin and antibiotic coprescription

Many statins are metabolized by cytochrome P450 isoenzyme 3A4 (CYP3A4). Drugs that inhibit CYP3A4 can, therefore, potentially increase the serum concentration of coprescribed statins. In a new study, coprescription of a CYP3A4-inhibitory antibiotics increased the risk of statin toxicity.

This study included 144,336 patients aged ≥65 years who were taking atorvastatin, lovastatin, or simvastatin. Data were collected from four databases, including details of hospitalization and outpatient prescriptions. Patients receiving a coprescription for an antibiotic were grouped into those receiving clarithromycin or erythromycin (CPY3A4 inhibitors) and those receiving azithromycin (which does not inhibit CYP3A4). Data on hopsitalization were examined in the 30 days after antibiotic prescription.

Coprescription of a CYP3A4-inhibitory antibiotic with a statin was associated

> “...CYP3A4-inhibitory antibiotics increased the risk of statin toxicity”

with a higher risk of hospitalization with rhabdomyolysis (absolute risk increase 0.02%, 95% CI 0.01–0.03%; relative risk [RR] 2.17, 95% CI 1.04–4.53), acute kidney injury (absolute risk increase 1.26%, 95% CI 0.58–1.95%; RR 1.78, 95% CI 1.49–2.14), and all-cause mortality (absolute risk increase 0.25%, 95% CI 0.17–0.33%; RR 1.56, 95% CI 1.36–1.80) than those receiving azithromycin and a statin. Hospitalization for hyperkalaemia, another prespecified outcome, was not affected by the type of antibiotic prescribed.

The diagnoses of rhabdomyolysis, acute kidney injury, and hyperkalaemia are dependent on the coding of laboratory results in the hospital databases. According to the investigators, patients with mild or moderate forms of these conditions might not have been appropriately coded in the hospital. Therefore, the data analysed in this paper are likely to be underestimates of the effect of antibiotics that inhibit CYP3A4 on statin toxicity.

The absolute risks of these adverse events are quite small, but physicians could consider a number of treatment options for patients taking statin therapy who require antibiotic treatment. Antibiotics that do not inhibit CYP3A4, such as azithromycin (used as the control in this study), might be prescribed. Alternatively, statin therapy could be temporarily stopped, or patients might be treated with a statin that is metabolized through pathways other than CYP3A4.

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Original article Patel, A. M. *et al*. Statin toxicity from macrolide antibiotic coprescription: a population-based cohort study. *Ann. Intern. Med.* **158**, 869–876 (2013)