A Timely Reminder About the Concomitant Use of Fusidic Acid With Statins

To the Editor—*Staphylococcus* species are a common cause of prosthetic joint infections, and among many older patients, long-term antibiotic suppression may be preferable to curative interventions involving multistage joint replacement. In countries where fusidic acid is available, a common oral suppressive regimen includes its use with rifampin [1]. Nevertheless, the use of such fusidic acid–containing combinations needs to be undertaken with some care due to the potential for important interactions with other drugs commonly used in this patient population, particularly lipid-lowering agents such as statins [2–9]. Although this problem was previously thought to mainly involve earlier statins (eg, atorvastatin, simvastatin), we now report a serious interaction with rosuvastatin, an agent being increasingly used due to its perceived low rates of adverse effects.

An 83-year-old man underwent a 1-stage total hip revision following an unsuccessful periprosthetic fracture repair. His medical history was significant for refractory chronic lymphocytic leukemia, chronic renal impairment (serum creatinine 170 umol/l), and ischemic heart disease, for which he was receiving metoprolol, aspirin, amlodipine, and atorvastatin. Intraoperative specimens grew methicillin-sensitive *Staphylococcus aureus* and he was started on vancomycin before changing to life-long suppressive therapy with oral rifampin (600 mg daily) and fusidic acid (500 mg twice daily) as further surgical management was not considered appropriate. Based on concerns raised by a review of online US pharmacy databases, his atorvastatin was changed to rosuvastatin to minimize any possible interaction with rifampin.

After 2 weeks in physical rehabilitation, the patient required urgent readmission with delirium, deteriorating renal function (potassium 7.0 mmol/L, urea 38.4 mmol/L, creatine 451 μmol/L) and severe rhabdomyolysis (creatinine kinase 11 627 U/L). Rifampin, fusidic acid, and rosuvastatin were ceased and vancomycin was restarted. Renal replacement therapy was commenced on day 4 due to oliguric renal failure, but the patient became profoundly hypotensive due to recurrent intestinal bleeding that failed to settle despite surgical intervention. Because of his overall poor prognosis, active treatment was withdrawn on day 12 and the patient died.

Rhabdomyolysis was attributed to either the change from atorvastatin to rosuvastatin or, more likely, the coadministration of fusidic acid with rosuvastatin. Further review of the literature revealed 25 cases of rhabdomyolysis with concurrent administration of fusidic acid with atorvastatin or simvastatin, probably via interaction at the CYP3A4 metabolism pathway [2–9]. However, there has only been 1 recent case possibly attributable to the combination of rosuvastatin and fusidic acid, with the mechanism remaining uncertain [9].

In the United Kingdom, avoidance of coadministration of fusidic acid with any statin has been recommended nationally since 2012 [9]. In the United States, fusidic acid is not yet available, and this is reflected in the lack of warnings regarding rosuvastatin in the current US online pharmacy databases.

Our case suggests that rhabdomyolysis induced by the combination of a statin and fusidic acid should be considered a class effect and not be based on specific statins. For short courses of fusidic acid,

a temporary cessation of statin therapy is probably the safest option. But for prolonged courses, such as those often used in bone and joint infections, very careful monitoring will be required or a nonstatin lipid-lowering agent used if lipid control is deemed sufficiently important [2, 9].

Given the imminent availability of fusidic acid in the United States, we believe this case provides a timely reminder of an important, potentially life-threatening drug interaction that should be considered when prescribing fusidic acid.

Note

Potential conflicts of interest. All authors: No reported conflicts.

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