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Statin-Associated Myopathy—An Elusive Clinical Problem

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Muscle disorders resulting from statin therapy, the most common manifestation of statin intolerance, are vexing to both patients and physicians. Statin-associated myopathy may appear as a spectrum of manifestations that include myalgias, myopathy, myositis, myonecrosis, and rhabdomyolysis.¹

Myonecrosis and rhabdomyolysis are uncommon, occurring in fewer than 1% of statin-treated patients, but myalgias and myopathy without creatine kinase elevation are reported in up to 5% of patients in clinical trials and in 25% or more in observational studies and clinical experience. To aid in the diagnosis of this often enigmatic condition, the American College of Cardiology provides a statin intolerance mobile app (<http://www.acc.org/statintoleranceapp>).

Risk factors include hypothyroidism, prolonged vigorous exercise, low levels of vitamin D, other underlying muscle disorders, coadministration of statins with drugs that inhibit cytochrome P450 3A4 (CYP3A4), and the specific statin prescribed (eg, fluvastatin sodium and pravastatin sodium are associated with a lower risk of muscle toxic effects).

Treatment options often begin with a drug holiday, which may lead to permanent drug discontinuation for patients with lower cardiovascular risk. For those who require ongoing low-density lipoprotein-lowering therapy, options include switching to fluvastatin, pravastatin, or ezetimibe; alternate-day therapy with rosuvastatin calcium; and discontinuing or modifying the dosages of drugs that inhibit CYP3A4, such as cyclosporine, amiodarone hydrochloride, and macrolide antibiotics.²

Continuing or modifying the dosages of drugs that inhibit CYP3A4, such as cyclosporine, amiodarone hydrochloride, and macrolide antibiotics.²

In this issue of *JAMA Internal Medicine*, Caughey et al³ provide evidence of an association between statin therapy and idiopathic inflammatory myositis (IIM), a specific muscle condition. Using a case-control design and data from an Australian myositis registry, the researchers found that cases of IIM had a significantly higher rate of statin exposure than population-based controls (adjusted odds ratio, 1.79; 95% CI, 1.23-2.60).

Proper interpretation of this study depends on 2 factors. First, the diagnosis of myositis must be histologically confirmed; in the study by Caughey et al,³ all registry patients had muscle biopsy-confirmed IIM. Second, exposure to statin therapy must be accurately classified. This study assessed statin exposure by different methods for cases (drug history in the medical record) and controls (prescription dispensing records), which may have resulted in misclassification bias. Thus, the association of IIM with statin therapy reported by Caughey et al cannot be considered definitive, although these are likely the best data currently available.

Statin-associated myopathy as well as muscular aches and pains will continue to be a concern to patients and a diagnosis elusive to physicians. This debilitating adverse effect underscores the importance of prescribing statins only to patients who will clearly have a net benefit.



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