

# Characteristics and Outcomes of Statin-Associated Myopathy

Hansen KE, Hildebrand JP, Ferguson EE, Stein JH. Outcomes in 45 patients with statin-associated myopathy. *Arch Intern Med* 2005;165:2671–6.

## Study Overview

**Objective.** To describe the characteristics and clinical course of patients with statin-associated muscle pain and weakness.

**Design.** Retrospective cohort study.

**Setting and participants.** Of 437 patients seen at a single academic medical center between 1990 and October 2003 with ICD-9 codes for myopathy, myositis, muscle weakness, or adverse drug reaction to a cholesterol-lowering agent, 45 were judged to have myopathy or myositis caused by statin treatment. Data from the case records of the 45 patients were collected using a standardized form. Patients were categorized as having clinically significant myopathy (creatinine kinase [CK] > 10 times the upper limit of normal with muscle weakness or pain), myositis (CK > 3 times the upper limit of normal with symptoms), or myopathy with muscle pain or weakness (CK ≤ 3 times the upper limit of normal or unknown).

**Main outcome measures.** Symptom characteristics and clinical course of statin-induced myopathy and response to statin rechallenge.

**Main results.** 8 of 45 patients (18%) had clinically significant myopathy. Symptoms occurred after a mean duration of statin therapy of  $6.3 \pm 9.8$  months. 37 (82%) had at least moderate muscle pain, and 14 (31%) had weakness. Pain was most commonly described as diffuse (36%), limited to the legs (27%), or occurring in the arms and legs (20%). 6 patients were hospitalized for treatment of rhabdomyolysis, and 1 patient with preexisting renal disease required permanent dialysis. Duration of statin therapy prior to the development of myopathy was shorter for hospitalized compared with nonhospitalized patients (mean, 1.3 versus 7.1 months;  $P < 0.05$ ). Coadministration of a statin with a drug known to increase the risk of statin-associated myopathy was common and occurred in 6 of 6 (100%) hospitalized and 17 of 39 (45%) nonhospitalized patients. The mean time to symptom resolution after statin discontinuation was  $2.3 \pm 3.0$  months, and 91% had no pain by 6 months. 37 patients subsequently received statin treatment after their initial episode of myopathy, in-

cluding 4 patients hospitalized for rhabdomyolysis. 57% developed recurrent muscle pain; 43% tolerated the statin (16 patients tolerated a different statin; 4 tolerated the same statin they had been taking at the time the myopathy developed).

**Conclusion.** Pain from statin-associated myopathy resolved when the statin was discontinued but frequently reoccurred if statin therapy was resumed. Six hospitalizations but no deaths attributable to statin-associated myopathy occurred at this medical center over a decade.

## Commentary

Serious muscle injury caused by statins is rare [1]. Rare events can be difficult to study, but searches of large clinical databases can facilitate these investigations if cases can be identified. The description of statin-associated muscle injury used by Hansen and colleagues is probably valid for patients with muscle symptoms severe enough to prompt patients to seek medical attention and receive a clinical diagnosis code related to muscle disease. This study's findings show that moderate-to-severe pain without weakness is common, although weakness was reported in a minority of cases. Cases of severe muscle injury seemed to present more quickly after commencing statins than cases of milder injury and were often associated with coadministration of drugs known to interact with statins. We can be reassured that the prognosis for this limited number of cases was generally favorable.

In interpreting this data, we should keep in mind that it applies to the era preceding the publication of several trials demonstrating the utility of high-dose statin therapy. Population-based safety studies are needed to determine if the frequency of statin-associated muscle injury increases as more patients are exposed to high doses (ie, atorvastatin 80 mg or simvastatin 80 mg daily) of potent statins.

This study design carries some important limitations. Because the medical record data used was not collected for research purposes, there could be inaccuracies in the characterization of patients' symptoms. Furthermore, some cases may have been missed. This seems especially true for mild cases and cases in which patients may have stopped statin treatment without seeking medical care.

### Applications for Clinical Practice

This study provides reassurance that statin-associated myopathy usually follows a benign course. Because all 6 cases requiring hospitalization involved coadministration of drugs known to increase the risk of rhabdomyolysis, continued caution is warranted in patients receiving polypharmacy, particularly when drugs such as gemfibrozil, verapamil, or diltiazem are used in conjunction with a statin. For patients at high cardiovascular risk who have recovered from statin-associated myopathy, re-trial with a reduced dose of

the same statin or switching to a different statin may be tolerated, but for many patients symptoms may reoccur and the second drug may need to be discontinued.

*—Review by Stephen D. Persell, MD, MPH*

### Reference

1. Graham DJ, Staffa JA, Shatin D, et al. Incidence of hospitalized rhabdomyolysis in patients treated with lipid-lowering drugs. *JAMA* 2004;292:2585–90.

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