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Potency Of Statins Linked To Muscle Side Effects

A study from the University of California, San Diego School of Medicine, published August 22 online by *PLoS ONE*, reports that muscle problems reported by patients taking statins were related to the strength or potency of the given cholesterol-lowering drugs.

Adverse effects such as muscle pain and weakness, reported to the U.S. Food and Drug Administration (FDA) were related to a statin's potency, or the degree by which it typically lowers cholesterol at commonly prescribed doses.

"These findings underscore that stronger statins bear higher risk – and should be used with greater caution and circumspection," said investigator Beatrice Golomb, MD, PhD, professor in the Departments of Medicine and Family and Preventive Medicine at the University of California, San Diego.

Golomb teamed up with researchers from California-based AdverseEvents, Inc., using the company's software platform to conduct a detailed examination of statin side-effect data from the FDA's Adverse Event Reporting System (AERS). The study analyzed muscle-related adverse events linked to each of the major statin drugs in total of 147,789 AERS reports, gathered between July 2005 and March 2011.

Looking at the most commonly used statins – both brand names and, when available, generic forms of the drugs – rosuvastatin, the strongest statin, had the highest rates of reported problems. This was followed by atorvastatin, simvastatin, pravastatin, and lovastatin.

"These rankings closely match the individual potencies of each statin. Thus, the strength of the statin drug appears to be a dominant factor in determining how likely muscle problems are to occur," said Golomb, who directs the Statin Adverse Effects Study at UC San Diego.

Rates were determined for each statin by tallying reports of muscle side effects, standardized to the number of prescriptions filled for that drug. This was done for individual muscle side effects, as well as for side effects overall.

Some experts have maintained that rosuvastatin, the strongest statin, should have superior safety, because it is less fat soluble, and was thereby assumed not to penetrate into muscle cells as much as other statins. In addition, rosuvastatin is not cleared by common drug-clearance pathways that are sometimes involved in adverse drug interactions.

“The FDA AERS data analyzed in this study, however, suggests that the higher potency of rosuvastatin may more than offset any safety advantages due to such factors,” Golomb said. She added that pooled analysis of statin studies in patients with stable heart disease do not indicate that higher strength statins result in a lower death rate. Therefore, “evidence showing that stronger statins may pose a greater risk of side effects is particularly important.”

“Post-marketed studies utilizing AERS data are becoming increasingly important to understand the lasting side effect risks of widely used medications in disparate populations. Until recently, conducting such studies has been difficult due to the fractured and inaccessible nature of the FDA’s raw data,” said Brian Overstreet, CEO of AdverseEvents. The study utilized the company’s unique data sourcing method called RxFilter™, which analyzed more than 140,000 AERS case reports filed with FDA over a six-year time period.

Statins are among the most widely taken prescription medications in the world, with over 30 million users in the United States alone and $19 billion in domestic sales. They are prescribed to lower cholesterol, and reduce the risk of cardiovascular disease. Their use has been linked to a variety of muscle-related side effects (together termed “statin myopathy”) that occur in as many as 10 to 15 percent of all statin users. These include commonly reported problems such as pain and weakness, as well as life-threatening muscle breakdown, known as rhabdomyolysis. Statin myopathies can significantly increase pain and injury risk and affect mobility, especially in older individuals.

“Only a fraction of adverse effects are reported to the FDA, and a range of factors can influence reporting rates and accuracy of this information,” Golomb said. “However, findings from this study align with – and extend— other forms of evidence.”

For instance, an earlier study from Golomb’s group at UC San Diego showed that patients with muscle problems related to statins often found relief from symptoms after stopping one statin. However, muscle pain or weakness consistently redeveloped if the patient was then placed on a higher potency statin, while patients placed on a lower potency statin had significantly lower risk of recurrence.

“Our findings suggest that individual statin potency is a critical determinant of how likely a statin is to cause problems,” Golomb concluded. “This information should help guide prescribing decisions for statins by offering more information on the risk-benefit profile of the class. It should also be important for guiding decisions about statin selection and use after a patient has experienced a muscle-related adverse event.”

Additional contributors to the study include Keith B. Hoffman, Christina Kraus and Mo Dimbil of AdverseEvents, Inc.
