Effect of Statins on Skeletal Muscle: Exercise, Myopathy, and Muscle Outcomes

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PARKER, B.A. and P.D. THOMPSON. Effect of statins on skeletal muscle: exercise, myopathy, and muscle outcomes. Exerc. Sport Sci. Rev., Vol. 40, No. 4, pp. 188–194, 2012. Statins are effective in reducing low-density lipoprotein cholesterol and cardiac events but can produce muscle side effects. We have hypothesized that statin-related muscle complaints are exacerbated by exercise and influenced by factors including mitochondrial dysfunction, membrane disruption, and/or calcium handling. The interaction between statins, exercise, and muscle symptoms may be more effectively diagnosed and treated as rigorous scientific studies accumulate. Key Words: cholesterol-lowering medication, muscle strength, aerobic capacity, myalgia, vitamin D, HMG CoA reductase inhibitor

INTRODUCTION

Hydroxy-methyl-glutaryl (HMG) Coenzyme A (CoA) reductase inhibitors or statins are the most effective medications for managing elevated concentrations of low-density lipoprotein cholesterol (LDL-C). These drugs also offer one of the most effective strategies in reducing cardiovascular disease and have been documented to reduce cardiac events in both coronary artery disease (CAD) patients (21) and in previously healthy subjects (3). Statins are so effective that they are presently the most prescribed drugs in the Unites States and the world.

Treatment guidelines based primarily on serum LDL-C levels were established by the National Cholesterol Education Program (NCEP) Adult Treatment Panel III in May 2001 (5). These guidelines suggest an LDL-C treatment goal of less than 100 mg·dL⁻¹ for patients with established vascular disease, diabetes, or a calculated 10-yr CAD risk of more than 20%. Several recent clinical trials support even lower LDL-C goals for many patients. The Heart Protection Study (HPS) observed a 23% reduction in CAD events among 20,536 high-risk patients treated with simvastatin 40 mg·dL⁻¹ for 5 yr (17). A similar percent reduction in cardiac events was seen in the 6793 patients whose baseline LDL-C was less than 116 mg·dL⁻¹. Moreover, an NCEP update stated that an LDL-C goal of less than 70 mg·dL⁻¹ is “a reasonable clinical strategy” for patients at very high risk of CAD and that older persons also benefit from LDL-C reduction. Recently published results from the JUPITER (Justification for the Use of Statins in Prevention: an Intervention Trial Evaluating Rosuvastatin) Trial indicate that healthy individuals without hyperlipidemia but with elevated high-sensitivity C-reactive protein levels benefit from a reduction in the incidence of major cardiovascular events after several years of treatment with 20 mg of rosuvastatin (22). These collective results suggest that increasing numbers of patients, including the elderly and those with low initial LDL-C levels, will be treated with larger doses of the more potent statins. Indeed, the Centers for Disease Control and Prevention reported that from 2005 to 2008, approximately 25% of U.S. adults older than 45 yr reported using a prescription statin drug in the last 30 d, a roughly 10-fold increase over 1988 to 1994 (Fig. 1).

MUSCLE SIDE EFFECTS ASSOCIATED WITH STATIN TREATMENT

Side effects are extremely well tolerated by most patients but can produce a variety of muscle-related complaints in some individuals. The most serious risk of these drugs is rhabdomyolysis with acute renal failure and even death. This risk was emphasized by the withdrawal of cerivastatin in August 2001 after the drug was associated with approximately 100 rhabdomyolysis-related deaths. Fortunately, clinically important rhabdomyolysis with statins is rare, with an overall reported incidence of fatal rhabdomyolysis of 1.5 deaths per 10⁵ prescriptions (27). Unfortunately, statins are much more frequently associated