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## Statins Shown to Cause Fatigue

In a study of more than 1,000 adults, researchers at the University of California, San Diego, found that individuals taking cholesterol-lowering statin drugs are more likely than non-users to experience decreased energy, fatigue upon exertion, or both. The researchers suggest that these findings should be taken into account by doctors when weighing risk versus benefit in prescribing statins.

Statin drugs are among the best selling and most widely used prescription drugs on the market. Recently, increasing attention has focused on statins' side effects, particularly their effect on exercise. While some patients have reported fatigue or exercise intolerance when placed on statins, randomized trials had not previously addressed occurrence of fatigue-with-exertion or impaired energy in patients on statins relative to placebo.



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In the June 11 issue of *Archives of Internal Medicine*, Beatrice Golomb, MD, PhD, associate professor of medicine at UC San Diego School of Medicine, and colleagues present randomized trial data which show that these side effects were significantly greater in persons placed on statins than those on a placebo.

More than 1,000 adults from San Diego were randomly allocated to identical capsules with placebo, or one of two statins at relatively low potencies: pravastatin (Pravachol) at 40mg, or simvastatin (Zocor) at 20mg – chosen as the most water-soluble and most fat-soluble of the statins, at doses expected to produce similar LDL (“bad cholesterol”) reduction. According to the researchers, the cholesterol reduction would be similar to that expected with atorvastatin (Lipitor) at 10mg, or rosuvastatin (Crestor) at 2.5-5mg.

Persons with heart disease and diabetes were excluded. Neither subjects nor investigators knew which agent the subject had received. Subjects rated their energy and fatigue with exertion relative to baseline, on a five-point scale, from “much worse” to “much better.”

Those placed on statins were significantly more likely than those on placebo to report worsening in energy, fatigue-with-exertion, or both. Both statins contributed to the finding, though the effect appeared to be stronger in those on simvastatin. (Simvastatin led to significantly greater cholesterol reduction.)

“Side effects of statins generally rise with increasing dose, and these doses were modest by current standards,” said Golomb. “Yet occurrence of this problem was not rare – even at these doses, and particularly in women.”

The magnitude of the effect observed can be seen in the research findings if, for example, 4 of 10 treated women on simvastatin cited worsened energy *or* exertional fatigue; 2 in 10 cited worsening in both, or rated either one as “much worse”; or if 1 in 10 study participants rated energy and exertional fatigue as “much worse.”

“Energy is central to quality of life. It also predicts interest in activity,” said Golomb. “Exertional fatigue not only predicts actual participation in exercise, but both lower energy and greater exertional fatigue may signal triggering of mechanisms by which statins may adversely affect cell health.”

For these reasons, the researchers state that decreases in energy, and increases in exertional fatigue on statins represent important findings which should be taken into account in risk-benefit determinations for statins. According to Golomb, this is particularly true for groups for whom evidence does not support mortality benefit on statins – such as most patients without heart disease, and women and those over 70 or 75, even if heart disease is present.

Additional contributors to the paper include Marcella A. Evans, Department of Anatomy and Neurobiology, UC Irvine; Joel E. Dimsdale, MD, UC San Diego Department of Psychiatry; and Halbert L. White, UC San Diego Department of Economics.

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