

First Comprehensive Paper on Statins' Adverse Effects Released

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A paper co-authored by Beatrice Golomb, MD, PhD, associate professor of medicine at the University of California, San Diego School of Medicine and director of UC San Diego's Statin Study group cites nearly 900 studies on the adverse effects of HMG-CoA reductase inhibitors (statins), a class of drugs widely used to treat high cholesterol.

The result is a review paper, currently published in the on-line edition of *American Journal of Cardiovascular Drugs*, that provides the most complete picture to date of reported side effects of statins, showing the state of evidence for each. The paper also helps explain why some people have a higher risk than others for such adverse effects.

"Muscle problems are the best known of statin drugs' adverse side effects," said Golomb. "But cognitive problems and peripheral neuropathy, or pain or numbness in the extremities like fingers and toes, are also widely reported." A spectrum of other problems, ranging from blood glucose elevations to tendon problems, can also occur as side effects from statins.

The paper cites clear evidence that higher statin doses or more powerful statins - those with a stronger ability to lower cholesterol - as well as certain genetic conditions, are linked to greater risk of developing side effects.

"Physician awareness of such side effects is reportedly low," Golomb said. "Being vigilant for adverse effects in their patients is necessary in order for doctors to provide informed treatment decisions and improved patient care."

The paper also summarizes powerful evidence that statin-induced injury to the function of the body's energy-producing cells, called mitochondria, underlies many of the adverse effects that occur to patients taking statin drugs.

Mitochondria produce most of the oxygen free radicals in the body, harmful compounds that "antioxidants" seek to protect against. When mitochondrial function is impaired, the body produces less energy and more "free radicals" are produced. Coenzyme Q10 ("Q10") is a compound central to the process of making energy within mitochondria and quenching free radicals. However, statins lower Q10 levels because they work by blocking the pathway involved in cholesterol production - the same pathway by which Q10 is produced. Statins also reduce the blood cholesterol that transports Q10 and other fat-soluble antioxidants.

"The loss of Q10 leads to loss of cell energy and increased free radicals which, in turn, can further damage mitochondrial DNA," said Golomb, who explained that loss of Q10 may lead to a greater likelihood of symptoms arising from statins in patients with existing mitochondrial damage - since these people especially rely on ample Q10 to help bypass this damage. Because statins may cause more mitochondrial problems over time - and as these energy powerhouses tend to weaken with age-new adverse effects can also develop the longer a patient takes statin drugs.

"The risk of adverse effects goes up as age goes up, and this helps explain why," said Golomb. "This also helps explain why statins' benefits have not been found to exceed their risks in those over 70 or 75 years old, even those with heart disease." High blood pressure and diabetes are linked to higher rates of mitochondrial problems, so these conditions are also clearly linked to a higher risk of statin complications, according to Golomb and co-author Marcella A. Evans, of UC San Diego and UC Irvine Schools of Medicine.

The connection between statins' antioxidant properties and mitochondrial risk helps explain a complicated finding that statins can protect against the very same problems, in some people, to which they may predispose others - problems such as muscle and kidney function or heart arrhythmia.

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