Quick quiz, what side-effects, if any, concern you about the use of statins, those medications designed to lower our cholesterol? Most people would mention the most common side effect, muscle aches or myalgia that occur in roughly 11% of patients [1]. How about a 28% increase in Type 2 diabetes among susceptible individuals taking a statin? People who develop diabetes or elevated cholesterol are fellow travelers sharing easily identified phenotypic risk factors, like body weight as well as more subtle, even clinically not apparent metabolic alterations. A new study tries to untie this Gordian knot of confounders.

The study is a retrospective review of Midwesterners with private insurance who underwent yearly examinations as part of their employee benefits. The study looked at 755 patients receiving statin therapy and an additional 3928 patients who were eligible for statin therapy but were not taking those medications. The groups were well matched concerning their demographics, LDL, and HDL levels. No patients, in either group had overt Type 2 diabetes, but in a significant limitation to the study, the subclinical markers of “pre-diabetes,” like an elevated HbA1c or elevated fasting glucose were not characterized. When followed for four years:

- 6.5% of patients on statins had developed a HbA1c over 6% compared to those not taking statins.
- Over the four years, 6.6% of all participants developed new-onset diabetes, but it was far greater in those taking statins, at 14.8%, than in those not on statins, at 5%.
- Neither the type of statin or the magnitude of the dose demonstrated any effect. There was a
trend suggesting that the occurrence of new-onset diabetes was related to an increasing period taking statins.

The study has limitations, but not characterizing the groups “pre-diabetic” markers casts a big shadow on their results. It joins a host of other studies and meta-analysis that raise but do not prove a tantalizing metabolic connection between our glucose and cholesterol metabolism where what’s good for one, may not be so suitable for the other. The FDA altered statin labeling [2] to reflect a concern for “incident diabetes and increases in HbA1c and/or fasting plasma glucose” based on their literature review but felt that statins benefits outweigh the risks.

The authors suggest that the underlying mechanism is the known reduction in coenzyme Q10 in patients taking statins. Coenzyme Q10 is involved in the creation of energy by our mitochondria, and because of the role of mitochondria in energizing our muscles, a deficiency of Coenzyme Q10 is hypothesized as part of the reason for statin’s adverse effect on our muscles. The impact altering mitochondrial energy production, in turn, alters fat metabolism, which in turn promotes insulin resistance, a known precursor to Type 2 diabetes. And while many recommend Coenzyme Q10 supplements, after all, “they had no known downside,” there is scant evidence that they correct myopathy let alone the heightened risk of diabetes.

The guidelines for statins are recommending increasing numbers of patients take this medication; the only fight is whether it should be 16% or 25% more patients. We are talking about say 9 million, and if this study is correct, that means we may be getting statins benefits along with say, a half million new unintended cases of diabetes. We don’t know. But do we have an obligation to perhaps determine whether statins for some underlying metabolic cause promote diabetes, and if that is the case, identify the patients at highest risk? Paving the road with statin’s good intentions may not be enough.


Source: Statin users have an elevated risk of dysglycemia and new-onset-diabetes Diabetes Metabolism Research and Review DOI: 10.1002/dmrr.3189

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