

Statins Linked With Heightened Aggression in Women, But Reductions in Men

By Michael O'Riordan, Medscape



A new study examining the effects of statin therapy on levels of aggression suggests that men and women may respond differently to the lipid-lowering medications^[1]. In men, statin therapy reduced aggression, particularly in younger men, but increased aggression in postmenopausal women.

The increase and decrease in aggression in women and men, respectively, was most consistent and significant among individuals with lower baseline aggression levels, report investigators.

"I don't think it's a very common problem," lead investigator Dr Beatrice Golomb (University of California, San Diego) said in reference to the extent of aggression/irritability among statin-treated patients. In her smaller clinical practice, Golomb said she encountered only a few patients with increased aggression after starting statins to lower cholesterol levels. That said, the "problem definitely occurs, and in some people it can be quite serious."

To *heartwire* from Medscape, Golomb explained that low cholesterol levels have been linked with aggression and to violent death/non-illness mortality, such as deaths from suicide, homicide, and accidents, in multiple observational studies. Efforts to lower cholesterol in animal models, such as monkeys, have also shown the animals behave more aggressively with lowered cholesterol levels. Case reports of individuals with aggression/irritability with statins have been documented.

Published July 1, 2015 in *PLoS One*, the University of California San Diego (UCSD) Statin Study included 1016 adults undergoing randomization to placebo, simvastatin 20 mg, or pravastatin 40 mg for 6 months with the intention of studying the noncardiac effects of statins. Aggression, measured using the Overt-Aggression-Scale-Modified (OASMa)—aggression subscale, was one of the primary end points.

Overall, the researchers observed a statistically significant sex-statin therapy interaction. In addition, the association between aggression and statin therapy also differed by patient characteristics, "which is true for many statin effects," said Golomb.

Older individuals and females treated with statins had less favorable outcomes, such as higher levels of aggression, compared with matched placebo-treated patients. In younger men, particularly those with lower levels of aggression at baseline, aggression levels were reduced on statin therapy compared with placebo, whereas for those considered more aggressive at baseline, as well as for older men, the association between statin therapy and aggression was less clear.

"Within men, we looked more specifically to see if we could identify factors that predicted direction and magnitude of effect," said Golomb. "We previously found that statins, on average, worsen sleep and lowered testosterone. Poor sleep has been linked with increased aggression, and lower testosterone has been linked with lower levels of aggression. In our study, both of those emerged as predictors, although the lack of sleep was a more robust predictor of aggression."

In women, treatment with statin therapy was associated with a trend toward increased aggression in the full sample of female participants. After researchers excluded females who underwent early or surgical menopause, the association with statin therapy and increased aggression was statistically significant compared with placebo. The increase in aggression in a typical postmenopausal group of females—age >45 years—was statistically significant in statin therapy vs placebo.

Clinically, Golomb said the most important take-home message relates not just to the study's findings. "Any time a behavioral problem arises de novo, medication should be suspected," she told *heartwire*. "And not just statins. There are other medications that can cause worsening irritability and aggression. One thing we don't emphasize enough in medical training is that when any new unexplained change arises in a patient, suspect the medication first. The [medication] represents something reversible, where if there is a cause the problem can be potentially fixed."

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