Hemorrhagic Stroke in the SPARCL Study

To the Editor:
Goldstein et al.\(^1\) reported a post hoc analysis of data from the Stroke Prevention with Aggressive Reductions in Cholesterol Levels (SPARCL) trial in order to determine the effects of high-dose atorvastatin in the secondary prevention of cerebrovascular events in men and women. However, they did not mention how statin therapy increased the risk of hemorrhagic stroke in men and women.

In fact, in the SPARCL trial as compared with placebo, the use of high-dose atorvastatin (in relatively young and accurately selected patients who had a stroke or transient ischemic attack) was associated with a 66% increase in the relative risk of hemorrhagic stroke among the patients receiving the statin drug.\(^2\) In clinical practice where atorvastatin might be given to older and unselected patients, this detrimental action might raise concerns both in women and men.

Indeed, in addition to treatment with atorvastatin, an exploratory analysis of the SPARCL trial found that having hemorrhagic stroke as an entry event, male sex, and advancing age at baseline accounted for the great majority of the increased risk of hemorrhagic strokes.\(^3\) However, a sensitivity analysis excluding all patients with a hemorrhagic stroke as an entry event in the SPARCL trial found that statin treatment was still associated with an increased risk of hemorrhagic stroke.\(^4\) Furthermore, in a subgroup of patients with a history of cerebrovascular disease enrolled in the Heart Protection Study\(^5\) which did not include patients with hemorrhagic stroke, a similar increased risk of hemorrhagic stroke during follow-up was demonstrated.\(^4\)

Of note, lower low-density lipoprotein cholesterol levels, with or without statin treatment, have also been shown to be strongly and independently related to a higher risk of symptomatic hemorrhagic transformation after ischemic stroke thrombolysis.\(^6\) Because only patients with nonfatal recurrence of stroke need recanalization, the higher risk of hemorrhagic transformation after recanalization therapy might be particularly detrimental in women, given that in the SPARCL trial nonfatal stroke was reduced in women by a nonsignificant 0.7%.\(^1\)

Therefore, we feel that in clinical practice there are still many concerns about efficacy and safety of high-dose statins in the secondary prevention of stroke.

None.

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